Testing of a Valsalva Assist Device (VAD) to assess effects on heart rate and strain pressures achieved compared to a standard manometer in healthy volunteers performing standard and modified Valsalva manoeuvres.

Isabel FitzGerald

Submitted by Isabel L FitzGerald, to the University of Exeter as a thesis for the Masters by Research in Medical Studies, June 2018.

(Signature) ……

Royal Devon and Exeter NHS

NHS Foundation Trust

Abstract

Background Supraventricular tachycardia (SVT) is a relatively common condition causing palpitations, which, if not treated, can have serious adverse effects. SVT can initially be treated with a Valsalva manoeuvre (VM) (an exhalation against resistance, similar to blowing up a balloon), which induces a vagal response (drop in heart rate), terminating SVT in 5-54%. The VM's efficacy is variable and there is debate as to the best way of generating the strain in practice and in which posture the VM should be carried out. A purpose-built device (Valsalva Assist Device (VAD)) has been proposed to improve this. We aimed to compare vagal responses of the supine and modified posture VMs using the VAD and standardised manometer.

Methods We performed a repeated measures randomised trial of four VMs (two supine VM and two modified VMs) in healthy adult volunteers with strains delivered using a manometer or VAD. Changes in heart rate were compared between the techniques. The pressure and duration of VM strains achieved with the VAD and manometer and adverse events were recorded and compared. The trial was registered with ClinicalTrials.gov (NCT03298880) and approved by the University of Exeter Medical School Ethics Committee.

Results 75 healthy participants aged 19-55 were recruited over three months. A mixed-effects linear regression was completed showing the modified VM had a significant drop of 7.7 bpm compared to the supine VM ($p<0.001$, CI 5.6 to 9.8). The VAD produced similar strain pressures but slightly shorter duration strains compared to the manometer.

Conclusions Modified VM was associated with a greater drop in heart rate than a supine VM. The VAD can be used to safely generate the recommended VM strain with equivalent pressure to the manometer but may require modification to enable the recommended duration of strain and full effect to be achieved.

List of Contents

List of Tables

List of Figures

Author's Declaration

All data collection was completed by me at the Clinical Research Facility in the Royal Devon and Exeter Hospital.

The statistical analyses were performed by Professor Paul Ewings.

Abbreviations

Abbreviation	**Definition**
AVNRT	Atrioventricular Nodal Re-entrant Tachycardia
AVRT	Atrioventricular Re-entrant Tachycardia
BP	Blood Pressure
mm	Millimetres
CSM	Carotid Sinus Massage
ECG	Electrocardiogram
ED	Emergency Department
HR	Heart Rate
mmHg	Millimetres of Mercury
NICE	National Institute for Health and Care Excellence
O_2sat	Oxygen Saturation
RCT	Randomised Controlled Trial
RR	Respiratory Rate
SVT	Supraventricular Tachycardia
VAD	Valsalva Assist Device
VM	Valsalva Manoeuvre

Acknowledgements

Firstly I would like to thank my supervisors Dr Andy Appelboam, Dr Iain Lang and Professor Paul Ewings, for all their help, guidance, patience and support throughout my project. I would also like to thank the National Institute for Health Research Exeter Clinical Research Facility and their staff for their support in conducting the study. With a special thanks to Anna Steele, and to the research staff of Rebecca, Chris, Dionne and Jo whom without, this project could not have been completed. I would also like to thank Gerens Curnow for undertaking the second read of the results.

This report presents independent research funded by University of Exeter supported by the National Institute for Health Research (NIHR) Exeter Clinical Research Facility. The views expressed are those of the authors and not necessarily those of the University of Exeter, NHS, the NIHR or the Department of Health.

Introduction

The Valsalva Manoeuvre (VM) is a safe, internationally recommended, first-line treatment for hemodynamically stable supraventricular tachycardia (SVT). (1,2) The VM is a simple technique of forced exhalation against resistance (similar to blowing up a balloon), which causes a reduction in heart rate mediated through the vagus nerve. Its success rate in clinical practice is variable (5-43%) with a very safe side effect profile. Achieving the best cardioversion rate possible is important as the usual second-line treatment (adenosine) typically requires hospital attendance, has significant side effects and is disliked by patients. (2,3) Adenosine pauses the heart and creates a sense of impending doom in the patients. (4)

The highest cardioversion rate achieved in clinical practice to date used a manometer controlled (40mmHg) strain and a modified VM (post strain leg elevation and supine positioning). However, the physiological advantage of this modification over a supine VM (currently the gold standard) has not been studied. VMs in clinical practice are often done incorrectly and usual methods of strain, such as using a syringe, are unreliable. (5) This is due to incorrect pressures being produced, which may not be as effective in activating the vagus nerve.

A purpose designed Valsalva assist device (VAD) would ensure a correct strain pressure is used, could carry instructions for the modified VM and could be kept by patients for immediate use should an attack recur. Evidence suggests that the earlier a VM is carried out, the more effective it is. (6) A VAD has recently been developed by Meditech and Andrew Appelboam but has not yet been tested in healthy volunteers.

We determined the efficacy of the modified VM and the VAD, by measuring their vagal response (decrease in heart rate) in healthy volunteers.

Aims and Objectives

Aims:

- This study aims to determine the physiological effects of a modified VM and evaluate the performance of a novel Valsalva assist device in healthy volunteers.

Objectives:

- To undertake a literature review answering three questions
    - What is the most effective type of VM?
    - How effective is the VM in terminating SVT?
    - How effective are current methods for strain creation?

- To evaluate whether there is a difference in vagal tone (drop in heart rate) in healthy volunteers performing a modified VM versus a standard supine VM.
- To evaluate the differences in vagal tone created by the VAD compared to the manometer.
- To measure and compare peak strain pressure and duration produced using the VAD compared to a standard manometer in supine and modified position.

Chapter One - Overview of Supraventricular Tachycardia and the Valsalva Manoeuvre

Supraventricular Tachycardia (SVT)

SVT is a disorder of the heart causing a substantial increase in heart rate due to the rapid generation of electrical impulses. This is caused by a small area of tissue or a distorted conduction pathway which creates an electrical circuit, often these involve re-entrant electrical activity. (7,8). These accessory pathways usually involve the atrioventricular node; this node is significantly affected by the autonomic nervous systems. (8) The incidence of SVT in America is 35/100,000 and is responsible for 50,000 emergency department visits annually showing that it is relatively common. It can also be a disabling condition. (9,10) These palpitations can be extremely distressing for patients, especially if they are experiencing them for the first time. SVT is a common presentation to ED, with an average of 50-100 patients per year in each UK emergency department (2) There is no standardised heart rate for the diagnosis of SVT as some people have SVT with a heart rate as low as 75, and the condition is diagnosed using an ECG. (11,7)

There are various types of SVT – Sinus Tachycardia, Atrioventricular Nodal Re-entry Tachycardia (AVNRT), Atrioventricular Re-entry Tachycardia (AVRT), Atrial Tachycardia, Atrial Flutter, Atrial Fibrillation, Inappropriate Sinus Tachycardia, Sinus Node Re-entry, Permanent Junctional Reciprocating Tachycardia, Non-paroxysmal Junctional Tachycardia, and Focal Junctional Tachycardia. (7) However, in practice, the term SVT is most often used to describe the more common Re-entry Tachycardia's AVNRT, AVRT and Atrial Tachycardia. Atrial Fibrillation and Flutter tend to be distinct diagnoses as they have more characteristic ECG features, do not respond to vagal manoeuvres and have different treatments. (12) This practical approach to the term will also apply in this dissertation.

Aetiology of SVT

Whilst some risk factors have been identified the underlying aetiology has not been identified. It has been shown that peak incidence of SVT presentation is in the middle decades of life (AVNRT at 48 range 30-66) years, AVRT at 36 (18-64). (13) SVT presents as palpitations and can cause a great decrease in a patient's quality of life. (7)

Types of SVT

Atrioventricular Nodal Re-entry Tachycardia (AVNRT)

AVNRT is a re-entrant circuit which travels through the posterior and anterior conduction pathways into the atrioventricular node (AV node). 25% of the population has two pathways inputting to the atrioventricular node, a fast conduction pathway and a slow conduction pathway. These two pathways form the re-entrant circuit. (7) SVT starts with an extrasystole (premature beat), during the refractory phase of the fast conduction pathway, causing the impulse to be conducted through the slow pathway. This impulse reaches the distal end of the tissue, where the fast pathway is ready to receive the impulse, so it conducts the impulse backwards (retrograde), now the proximal part of the slow pathway is repolarised (due to short refractory period) and can be stimulated again. This is how the circuit starts and the impulses continue round the short and fast pathway creating the typical re-entrant circuit. (14) The atypical re-entrant circuit is formed when the impulse travels in the opposite direction. These differences are demonstrated in different ECG morphology; typical AVNRT has invisible p waves as they are hidden within the QRS complex, where atypical AVNRT produces inverted p waves typically in the middle of or late in the RR interval. (7)

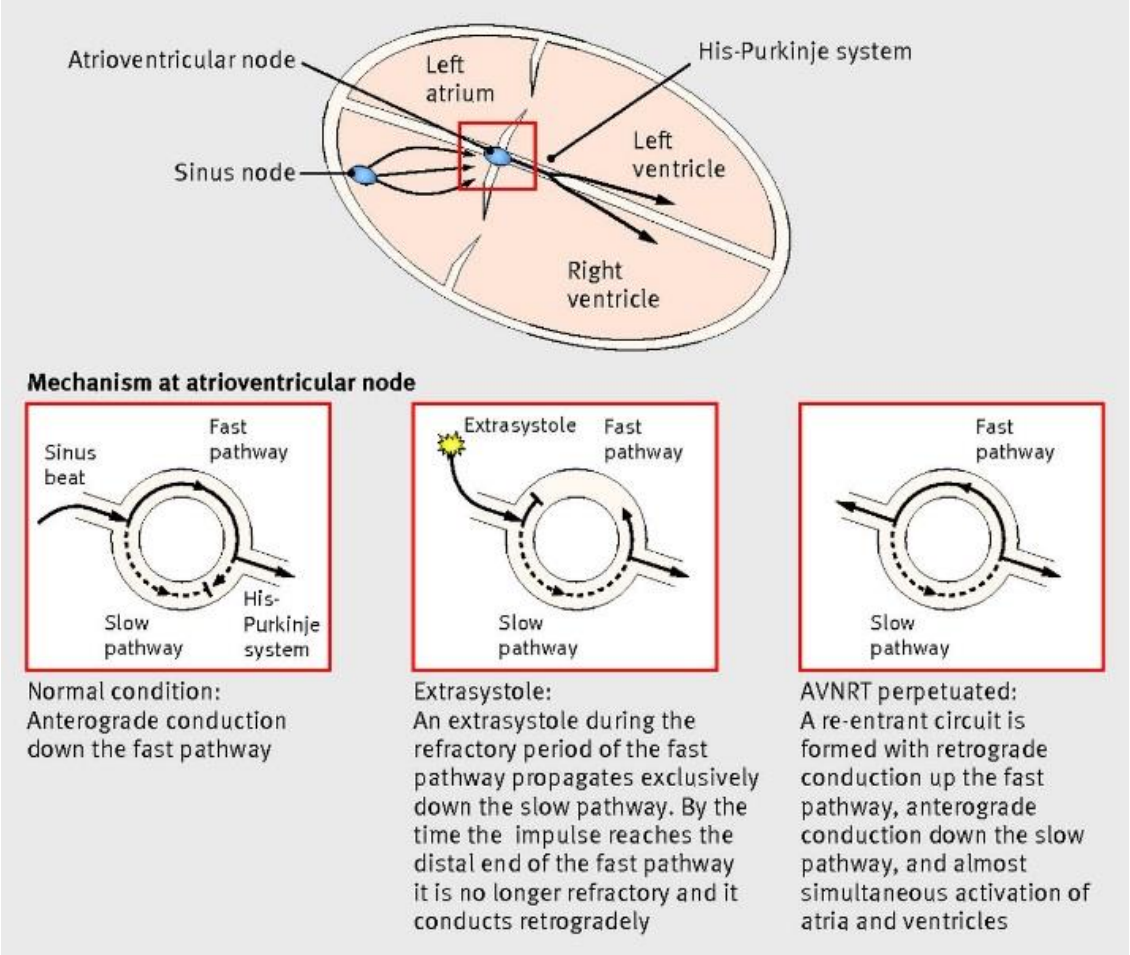

Figure 1 Mechanism for Atrioventricular Nodal Re-entry Tachycardia (7)

Atrioventricular Re-entry Tachycardia (AVRT) (including Wolff-Parkinson-White syndrome)

This re-entrant pathway requires the presence of an accessory pathway; this is a small strand of myocardium that bridges the atrioventricular insulation, which causes pre excitation of the ventricle as it is conducted more rapidly through this section than through the AV node. (15) This early ventricular activation manifests as a delta wave (upstroke in the QRS complex), however this is not always present. (7,16) These pathways can conduct in both directions, and the pre-excitation varies depending on the time required to cross the AV node and location of the accessory pathway. Differing from the AVNRT this arrhythmia is triggered by an extra atrial systole (premature beat from atria) that finds the accessory pathway refractory due to the normal impulse having just been conducted. Therefore, the impulse is transmitted down the AV node and then up the accessory pathway. This is where the circuit starts and continues as the

impulse is transmitted from the accessory pathway to the AV node continously. (7)

Atrial Tachycardia

Atrial tachycardia is the result of an abnormal impulse formation or re-entrant mechanism. These are usually classified by their origin within the atrium, e.g. focal atrial tachycardia or macro re-entry. (7) It can be hard to distinguish atrial tachycardia from other types of SVT on standard ECG investigation. This causes these rhythms to be commonly managed in the same way at least initially, in the emergency department (ED). Due to the low proportion of atrial tachycardia in SVT, there is little reason to distinguish it quickly in ED. (2)

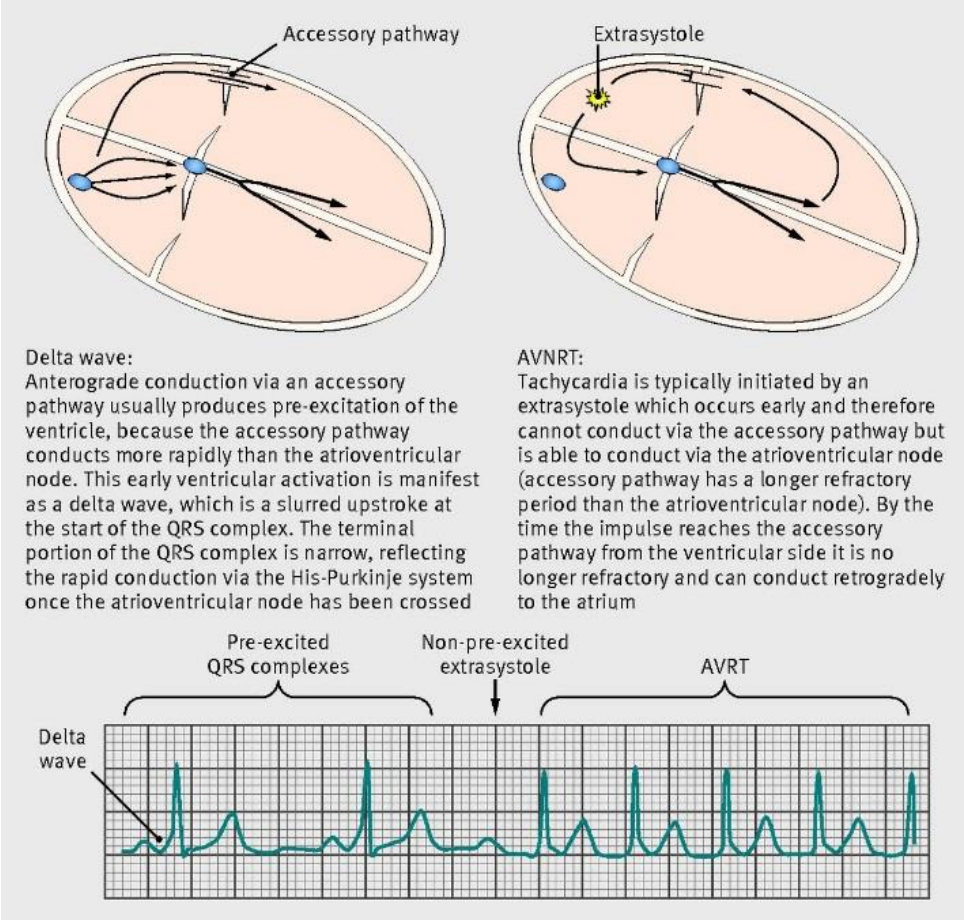

Figure 2 Mechanism for Atrioventricular Re-entry Tachycardia (7)

The current first line treatment for terminating SVT is the Valsalva manoeuvre. I will discuss this manoeuvre below.

Valsalva Manoeuvre

The first line treatment of SVT is the VM. The Valsalva manoeuvre (VM) is a short (15 seconds) strain similar to that of bearing down or blowing up a balloon, which increase intrathoracic pressure (40mmHg). This in turn causes a complex physiological reactions resulting in a rise in blood pressure and a drop in heart rate; it can also give important diagnostic information in the case of atrial tachycardia (exposing p wave morphology). (17,7,2) It is inferred that those VMs that produce the most significant fall in heart rate have the largest vagal tone and will therefore have the highest chance of conversion from SVT to sinus rhythm. (8)

The 40mmHg strain for 15 seconds is the simplest VM and is currently standard practice; it is achieved by blowing into a standard manometer or syringe in the supine position. This method of creating the VM is the NICE recommended first-line treatment for SVT. (17) Using the most effective method of VM is essential, to increase the chances of a successful termination of SVT and reduce the need for other interventions. (18) The optimal technique has been debated, and different techniques trialled to find the best. Recent studies have demonstrated that a postural modification of the VM has a better outcome for terminating SVT. (18) This technique is termed the modified VM. This is where a patient carries out the Valsalva strain for 15 seconds at 40mmHg in a semi-recumbent position (45-degree angle). Immediately at the end of the strain, they are laid flat and have their legs raised at 45-degrees for 15 seconds before returning to a semi-recumbent position as shown in figure 3. (2)

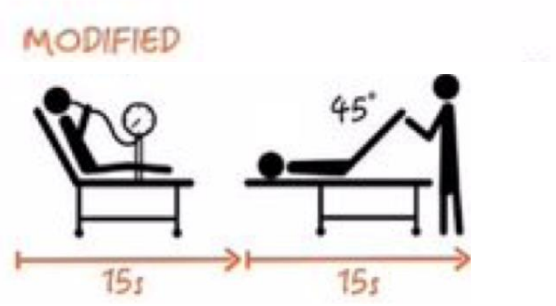

Figure 3 The Modified VM (19)

The VM is one of the best treatments available because it is inexpensive, non-invasive and easily reproducible with minimal side effects. (20) The use of VM has been shown to reduce complications of drug therapy without changing the number of treatment failures. (3) It is shown to be frequently effective in the termination of SVT, and if immediately undertaken can prevent the need for hospital admission. (8)

History of VM

There is some controversy about the origin of the VM, but it is thought to be first described by Antonio Valsalva in 1704, in Italy. (21) Its earliest description involved occluding mouth and nostrils as the air was compressed inwardly, it was claimed to expel pus from the middle ear. Valsalva postulated that this procedure would cause the expulsion of abnormal cerebral matter either via the wound, mouth or the auditory meatus. (21) This he believed possible due to the presence of a foramina between the ear and the cranial cavity. However, there is some controversy whether this is the first definition of a VM, as in 1497 Leonard of Bertapaglia described a similar phenomenon thought to be able to detect skull fractures. (22)

There are also hints of the origin of vagal manoeuvres in ancient Egyptian healing practices, though this has not been proven. The VM was largely forgotten until 1859 when Weber showed the VM was able to interrupt his pulse. However, his experimentation was stopped when he developed convulsions while demonstrating this manoeuvre to a crowd. (23) This was probably an early illustration of the risks involved in prolonged reduction in venous return, causing cerebral hypoxia. (24) In 1913 it was proposed that stimulating the vagus nerve by pressure, e.g. carotid sinus massage would terminate the paroxysmal tachycardia. (25) Cohn reviewed the evidence for the efficacy of vagal manoeuvres in 1913 and found it was mixed and viewed with mistrust. Cohn stated that while carotid sinus massage was effective, another manoeuvre seemed to be more effective, this he described as a deep respiratory movement which we are led to believe is a VM. (25) The evidence shows that using vagal

stimulation to terminate tachycardia has been around for a long time, though its use has never been widespread before due to its lack of efficacy.

Uses of VM

The VM has been used for a variety of different reasons, most commonly for termination of SVT, assessment of heart disease and autonomic nervous system functionality. (20) In cardiology and urology, it can be used diagnostically in conjunction with other examinations, to assess heart failure and incontinence. (26) Heart failure is assessed in two ways either using a doppler or by assessing the heart rate response during a VM. There is no tachycardia during the strain phase of the VM in heart failure; ventricular rigidity means that changes in preload do not affect the stroke volume, causing no change in heart rate. (26) The VM is used to assess the extreme values of intrastrain tachycardia and post strain bradycardia, which is used to quantify autonomic nervous system failure. (27,28) This is important as these conditions can affect the efficacy and safety of the VM in terminating SVT.

Although the most common use of the VM is the management of supraventricular tachycardia, variations are used by other specialities. ENT specialists use a form of VM against a closed glottis (to test Eustachian tube function) which does not raise intrathoracic pressure so, therefore, it is not a true VM. (28,29)

Physiological Effects of VM

To understand why the VM is effective at terminating SVT, we must first explore the physiology underlying the VM. The most critical physiological effect is the bradycardic response. (30) In the past, there has been controversy about the physiological effects caused by the VM. This reflects the complex mechanisms involved in the physiology of the VM. (30,22) This intricate process includes a hemodynamic and autonomic response which can be divided into five phases. (30)

Phase zero is the intake of breath before the VM and is therefore sometimes not included. This breath causes an initial decrease in intrathoracic pressure, causing a compensatory fall in arterial pressure. (30)

Phase one is the onset of the strain, where the pressure of the thorax is increased causing a rise in blood pressure and causes a transient slowing of the heart rate. This is due to the intrathoracic pressure causing a direct mechanical effect on the heart and intrathoracic blood vessels. (31,30)

Phase two is the end of the strain, where the pressure in the abdomen and thorax rises causing a significant decrease in venous return, and therefore reducing left ventricular preload, causing a consequential decrease in stroke volume resulting in a drop in blood pressure. (32) This causes a reflex rise in heart rate and peripheral vascular resistance taking place about 7 seconds into the strain, which gradually brings the blood pressure back to baseline, due to this increased sympathetic activity. (28,30)

Phase three is the release of the strain causing a decrease in intrathoracic pressure leading to an instant drop in blood pressure. However venous return is recovered and blood flow increases, improving diastolic filling and stroke volume. This increased stroke volume is pumped into the increased vascular resistance (vasoconstricted vessels) causing a spike in blood pressure. (31,30)

Phase four shows the blood pressure overshoot, triggering the carotid sinus receptors reflex, which excites the vagal nerve increasing vagal tone causing a decrease in heart rate, although the blood pressure remains high for some time this is thought to be due to adrenal medulla hormones, as the sympathetic nerve activity is low. (28,30,31,33,27,26)

Previous studies have shown that increasing the refractoriness of the AV node with vagal stimulation can terminate SVT. It was shown that the response rate was related to the level of vagal reaction. (34)

Physiological Effects of Modified VMs

There have been various attempts to modify the VM over the years to increase its utility in everyday practice. This section will review the physiology behind the supine VM, Trendelenburg VM, erect VM, sitting VM, semi recumbent VM and the modified VM.

Currently, the gold standard VM is the supine position; this is thought to be better due to increasing a patients' vagal tone and reducing the sympathetic response. Increasing venous return during phase four will increase the vagal response causing a more significant bradycardic effect. (35) A recent study done in children with SVT examined a modification to induce a more significant vagal response. The technique assessed patients that were turned upside down or did headstands and showed a cardioversion rate of 67% vs 33% compared to standard VM on the first attempt. This supports the evidence behind the idea that increasing the venous return increases the vagal tone and rate of cardioversion. (6)

The Trendelenburg VM is when a patient lies supine with their head tilted down 10-15 degrees. The Trendelenburg modification was thought to work on a similar principle as the supine VM that the head down position would increase vagal tone increasing the bradycardic response, however it has not been shown to be an improvement. (35,18)

The erect position (standing) of the VM is much less effective compared to the supine VM and is thought to be due to raised sympathetic tone blunting baroreflexes. (36,37) This study showed that the heart rate increased with increased orthostatic pressure due to the fall in blood pressure, this reduces

conduction to the glossopharyngeal and vagal nerve. This occurs in conjunction with the activation of the adrenergic system, leading to increased vascular resistance. This causes a beta blockade, which blunts the baroreflexes, resulting a decrease in vagal nerve stimulation.

Other positions which have been reviewed are the semi-recumbent position and sitting position. Both of these have been shown to be less effective than supine VM. (8) This is thought to be due to blood pooling in the legs causing larger basal sympathetic tone, causing a reduced vagal response. The surge in venous return that precipitates the vagal response is also diminished due to gravitational forces in sitting and semi-recumbent positions. It is important to know that the supine position was significantly more effective compared to the semi-recumbent position. (8)

The modified VM with leg raise should have the greatest effect, due to the increased the venous return post VM strain, therefore causing an exaggerated overshoot in blood pressure in phase three. (8) In turn, this results in a more profound activation of the vagus nerve and a greater corresponding drop in heart rate. This theory is supported by studies showing that the standing VM is less effective at terminating SVT, only terminating 20% compared to 54%; this is thought to be due again to the higher sympathetic tone. (37) The modified VM was shown to be very effective compared to the semi-recumbent VM. (2,8)

Variables which influence the VM

The VM is a complicated process of neural and hemodynamic changes. A variety of factors affect the performance of the VM, other than have already been stated such as; volume and rate of the pre-strain breath, extent and rate of strain pressure increase, changes in lung volume and strain pressure, duration of the strain period, depth and rate of the post strain breathing. (30) Conditions that influence venous blood return during the VM might also affect the manoeuvre's efficacy.

Pre-strain breath

This breath affects the VM as it determines the volume of the lungs and therefore the intrathoracic blood at the onset of the VM; this affects not only straining forces. (30) The changes in intrapulmonary blood have an enhanced effect on phase two of the VM, as they can cause a bradycardic response rather than a tachycardic response. (30) However, it has a minimal effect on phase four and one, making it less relevant to this dissertation, which is concerned with the bradycardic phases only as this is where most SVT terminations take place.

Strain pressures

This force of strain determines the intrathoracic pressure during the VM. It can be accurately measured, using a manometer, if the glottis is open while undertaking the strain. However, it is possible to produce the pressure using mouth pressure only (having a closed glottis) and therefore no intrathoracic transmission of pressure. This would not result in the classic VM phases and bradycardic response. (27) This is prevented by creating a small air leakage as pressure is quickly lost from the small volume of the mouth with such a leak but can be maintained with intrathoracic volumes. It is crucial, this leak is not excessive, as this would cause a drop in the intrathoracic pressure as the lungs vital capacity volume is lost. (27) Pressures of 30mmHg or lower have been shown to be ineffective at creating a VM. (22) The Ekinici study explored variation in pressures and found that there was no statistical significance between doing the VM at a pressure of 40 compared to 50mmHg. (38) If a pressure higher than 50 is used, there is a increased chance of syncope and other potential complications due to the drop in venous return being too large, reducing cardiac output and cerebral perfusion as demonstrated dramatically by Webber. (23,22)

Duration of pressure

The duration of 15 seconds has been used in previous studies that have demonstrated the effectiveness of the modified VM in SVT. (2) It reduces the intra strain tachycardia and replaces it with a steep rise in blood pressure ensuring a more significant and more prolonged post strain bradycardia. (18,8,27)

Few studies have compared the 15 second strain to other lengths; the Ekinci study compared a 10 second strain to the 15 second strain and found no difference. (38) This was followed by the Mehta study showing that the 15-second manoeuvre produced a greater vagal response compared to the 30-second manoeuvre. (37) Strains longer than 15 seconds have not been shown to have any advantage. They also have a larger theoretical risk of increasing side effects due to a prolonged drop in venous return reducing cardiac output, so shortest strain while maintaining efficacy should be used. (39,22) With strains longer than 15 seconds, it becomes harder for patients to hold the strain for the full length of time. A strain of greater than 20 seconds produces a more gradual reduction in heart rate compared to the more abrupt drop with the 15 second strain. (30)

If there is a significant air leak in the VAD, patients may be unable to complete the 15 second strain preventing all phases of the VM being seen. (27) However, there is some evidence suggesting that a 10 second strain is all that is needed, so even if there is a leak, the strain will hopefully still be produced. (39)

Baseline heart rate

The baseline heart rate is highly variable between individuals and continuously under influences from internal and external stimuli. (27) It is essential to attempt to stabilise the heart rate before initiating the VM in experimental procedures whereas in spontaneous SVT this is not required. There should be enough time to allow participants to return to their resting heart rate. (27)

Stimulants and Obesity

Evidence shows that a participant's response to the VM is reduced if they have consumed energy drinks in the last 60 minutes. (40) Energy drinks contain large quantities of caffeine which has been shown to affect the autonomic system. The caffeine causes an increased catecholamine release increasing the sympathetic innervation, therefore reducing the effect of a VM stimulating the vagal response. (40) Obesity was also shown to negatively correlate to the physiological drop in heart rate, though this effect is smaller than that of caffeinated drinks. (40)

Gender

Gender was shown not to have an effect on the VM in terminating SVT. (37) However several studies show there are more women compared to men with SVT. (34,3)

Age

The Valsalva ratio is negatively correlated with age (p 0.06). (37) This is thought to be due to a decline in autonomic tone with increasing age, therefore meaning the VM is more successful in younger participants. (37)

Treatment of SVT

The underlying principle in the treatment of SVT is to slow conduction through the AV node, through the action of the vagus nerve. Activation of the vagus nerve causes a pause long enough to interrupt the re-entrant electrical activity. (8) This allows the underlying sinus node activity to become the only activity, and normal sinus rhythm is restored. (8) This is why NICE (The National Institute for Health and Care Excellence) recommends vagal manoeuvres as the first line treatment of SVT. (17) There are 3 main types of vagal manoeuvres including VM, carotid sinus massage and facial ice water immersion. It is discussed below why the VM is superior to these other vagal manoeuvres. The second line management is the use of a drug called Adenosine which is discussed below.

For the management of SVT, it is important to assess the patient's haemodynamic stability because if the arrhythmia is poorly tolerated it can cause hypotension (low blood pressure). If a vagal manoeuvre is performed on these patients, it can cause a further drop in cardiac output, resulting in worsening perfusion and syncope. For unstable patients, therefore, immediate chemical or electrical cardioversion is recommended. (7)

Evidence behind the VM

Examining previous evidence of patients whose SVT terminated, there were differences in which phase of the VM the termination occurred, this was associated with the type of SVT. (37) Of those who had AVRT antegrade terminations, 11% occurred in phase one and 89% in phase four. Whereas in retrograde termination of their SVT 94% occurred in phase two. (34) However, those with AVRNT retrograde termination, 100% occurred in phase two. This differs from antegrade termination where 86% terminated in phase four and 14% in phase two. (34) In AVRT the number of people with retrograde terminations was almost half of that of those with antegrade terminations, however, they are almost equal in AVRNT. (34) It is unknown, but this may be why VM is less effective in AVRNT compared to AVRT. We measured the bradycardic response because it is where the majority of SVT termination occurs.

Evidence has shown that the quicker VM is undertaken, the greater the likelihood of SVT termination. (8) This, not only reduces the need for antiarrhythmic medication (with greater side effects) but also prevents venepuncture and other potential complications from being in the hospital. (8)

Evidence of other vagal manoeuvres compared to the VM

VM vs Carotid Sinus Massage

The most common vagal manoeuvres are the carotid sinus massage and the VM. (17) Previously it was thought these two manoeuvres had a similar rate of termination. (3) However, it has now been shown that the VM is much more effective than the carotid sinus massage, which is of very limited use. (41,42,43,44) Analysing various papers the rate of conversion was in the range of 5-54% for the VM compared to 0-17 % for the carotid sinus massage. (45,41,3,34)

The literature on this topic indicates mixed results. A seminal paper by Lim showed that the VM and carotid massage have more similar rates of SVT termination (average success rate 18% and 11.8%) than otherwise shown in the literature. However, this could be due to the method of VM (40mmHg for 30 seconds at a 90 degree angle) which has been shown to be less effective. (3)

Taylor found a low rate of cardioversion with the VM at of 6.1%; this was superior to carotid sinus massage at 2%. (46) These results show a lower termination rate for VM than otherwise seen. This may be due to two things firstly the very small sample size of 18 people receiving VM and 13 receiving carotid sinus massage. Secondly, it is not stated how the VM was performed which greatly affects its efficacy.

The most significant difference is shown in the Mehta study in which the VM converted 54% compared to 17% ($p<0.001$). This study was done on patients with a history of SVT who had it electrically induced for the trial. (37) This may

have made the patients easier to treat and so explain why it is more successful. However, the difference is marked and shows how much more effective the VM is. The ratio of the pre valsalva to post valsalva heart rates (valsalva ratio) was shown to be significantly higher in patients undergoing the VM compared to carotid massage (p=0.001). (37)

The major downside of carotid sinus massage compared to VM is the greater number and severity of side effects including carotid atheroembolism, ventricular arrhythmias and stroke. (37) A recent article suggests that the neurological complication rate may be as high as 1%. (43) The efficacy of carotid sinus massage is dependent on pressure and correct direction of the pressure on the carotid sinus (operator skill). (3,47) The major risk of side effects and reduced effectiveness compared to the VM is the main reason the use of VM is supported in preference to the carotid sinus massage, as a first line treatment for SVT. (43)

VM vs Facial Ice Water Immersion/Human Dive Reflex

Facial Ice Water Immersion and Human Dive Reflex both result in cold-induced bradycardias. However they are the least common vagal manoeuvre used in adults. The human dive reflex (HDR) is thought to be similar to that of seals used to slow their metabolic and heart rates to enable long dives. (18) This treatment is popular in babies and infants with SVT, however, in adults it has been shown to be not very effective. The Mehta study showed that face immersion was worse than carotid sinus massage with a termination rate of 17% compared to 23%. (37) Smith and Broek also showed that the VM was significantly better than the HDR $p<0.001$. (18)

Pharmacological Treatments

If vagal manoeuvres are unsuccessful, the ACC/AHA/ESC guidelines recommend adenosine as first-line medication. (7,1) This is due to its short half-life, quick action and effectiveness. It has been shown to terminate SVT in up to 91% of patients. (7) Adenosine works in similar ways to the VM by causing an atrioventricular nodal block; which blocks the refractive pathway and therefore

inhibits the re-entrant circuits. (48,49) Though adenosine is very effective it has unpleasant side effects for patients including dyspnoea, flushing, chest pain and most notably transient episodes of bradycardia. The latter can cause intense anxiety with many patients reporting the treatment is very unpleasant (sense of impending doom, or that they are about to die). (49,2,48) Like other anti-arrhythmic drugs adverse events can occur and include arrhythmias, most commonly premature ventricular or atrial complexes but it can also trigger non-sustained ventricular tachycardia, atrial fibrillation. (10) Alongside this its bradycardic effect can cause more serious bradyarrhythmias especially in patients with sinus node dysfunction. (49) Due to possible bronchospasm Adenosine is contraindicated in patients with unstable asthma. In contrast, the VM is well tolerated, felt to be very safe and so it is so important to optimise the efficiency of the VM to reduce the use of adenosine or other pharmacological interventions. (50)

If the first dose of 6mg adenosine does not terminate the arrhythmia, another 12mg of adenosine is given, if still no cardioversion another 12 mg is given. (51)

Other pharmacological interventions are administered if adenosine fails but are not in common use. These include verapamil, metoprolol, amiodarone or lidocaine. (52)

Long-term Management for SVT

Patients who have suffered an SVT frequently experience recurrences. For these patients, there are interventions that can reduce the frequency of attacks. Lifestyle changes, including reductions in the consumption of caffeine, alcohol, and cigarettes, as well as good levels of rest, have all been shown to reduce the frequency of SVT episodes. Medical management, including through beta-blockers, verapamil, and digoxin, can also be considered. Finally, catheter ablation has been shown to cure 95% of recurrent SVT's, though this is not without risk and is therefore used only following unsuccessful management with conservative and medical approaches.

Often the patient will have recurrent SVT, in these cases, specific interventions can help. The first intervention is lifestyle changes, cutting down caffeine, alcohol, cigarettes and ensuring the patient get enough rest. If this does not improve the patient's symptoms, the patient is given rate control medications, e.g. beta-blockers, verapamil and digoxin. If medication does not improve symptoms or is not tolerated, catheter ablation is used and cures 95% of SVT. However, it does have significant risks which is why it is the third line treatment, although in some practices it is used much earlier due to its more definitive actions. (53,54)

Chapter Two - Literature Review of the Valsalva Manoeuvre's Effectiveness

Introduction

This chapter evaluates the efficacy of the VM using all levels of evidence. This review has two sections: section one examined the effectiveness of VM and its modifications, and section two examined the effectiveness of current strain creation. We are assessing whether the VM is a viable and effective first line treatment and whether it is possible there are improvements that could make it more effective.

Method for Literature Review

I initially explored the latest management of SVT using the BMJ and other clinical review articles for background information. I then searched for papers from August 2017 to May 2018, regarding the Valsalva manoeuvre using the TRIP, PubMed, ResearchGate, and Google Scholar databases. I used the Zetoc Alert system to inform me of any new studies. A Boolean search was completed using the following search terms: Valsalva, SVT, supraventricular tachycardia, syringe. I also searched ClinicalTrials.gov for any ongoing studies.

All papers that discussed the VM, its physiology, effect, creation or use were identified and screened. The references of recent studies were also searched for studies that may have been previously overlooked.

Inclusion criteria for section one required the use of the VM on either healthy volunteers or on patients experiencing SVT. The inclusion criteria for section two required the assessment of strain production for a VM and assessment of the ability of health professionals to produce a VM. Both sections were restricted to those written in English and papers published from January 1985 to May 2018. Papers describing other uses of VM not relevant to our study were excluded.

Section One Identification of Papers

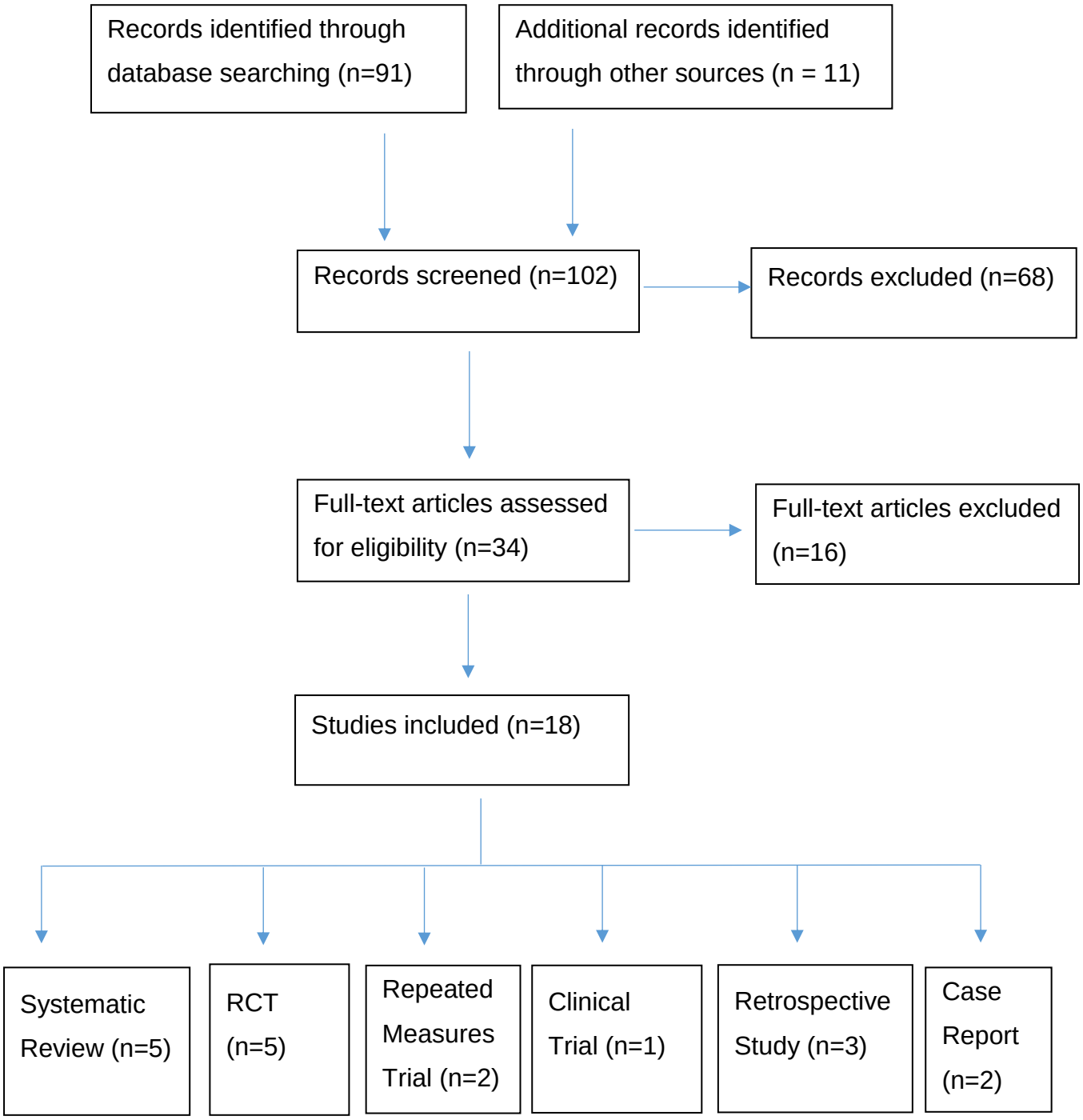

Figure 4 Method for Section One Literature Review

Section Two Identification of Papers

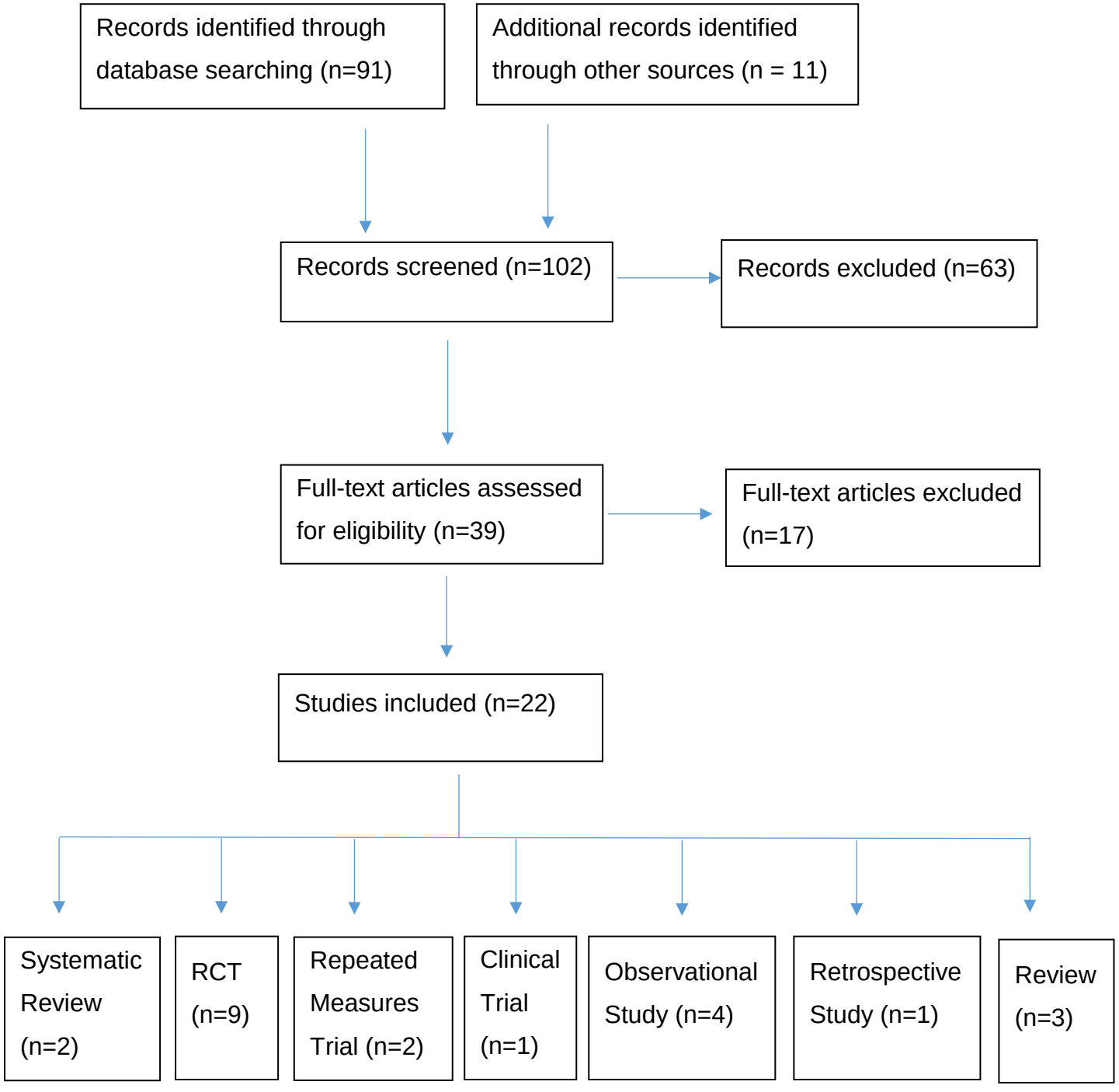

Figure 5 Method for Section Two Literature Review

Section One – Is the VM effective in terminating SVT?

Efficacy of the VM

The studies identified are shown in tables 1 and 2. The search identified three types of evidence:

1. Clinical trials in patients presenting with acute episodes of SVT
2. Trials conducted in the electrophysiology laboratory with induced SVT
3. Systematic reviews

Table 1: Critical Appraisal of Clinical Trials in Patients Presenting with Acute Attacks of SVT

Name/ Author	Type of Trial	No of people	Subject	Key Findings	Positive attributes	Critical Appraisal
REVERT (2)	RCT	433	Modified VM vs semi-recumbent VM.	Modified VM terminated SVT in 43% patients with 17% being terminated in the semi recumbent position.	Large population, randomisation, clear endpoint, nonstandidised leg raise-normal practice, 164 different clinicians delivering treatment -increases external validity, patients blinded to treatment and control, intention to treat analysis	Clinicians could not be blinded to treatment due to nature of treatment.
Corbacioglu (55)	RCT	56	Modified VM vs sitting VM.	Modified VM had a termination rate of 42.9% compared to sitting VM 10.7%.	Randomisation, clear endpoint.	10ml syringe used, small population, no blinding.
Montemdei (56)	RCT	100	Handheld manometer supine VM, assessing factors for successful reversion	SVT was terminated by VM in 14.8%, biggest factor for successful termination was having had SVT previously.	Randomisation	No control group, no blinding or comparison made. 55 participants had induced SVT for the study, used VM 30-50mmHg, no blinding

Table 1 Critical Appraisal of Clinical Trials in Patients Presenting with Acute Attacks of SVT

Table 2: Critical Appraisal of Clinical Trials in Patients Presenting with Acute Attacks of SVT

Name/ Author	Type of Trial	No.	Subject	Key Findings	Positive attributes	Critical Appraisal
Lim (3)	Clinical trial	148	VM vs carotid sinus massage.	VM had an overall success rate of 18% compared to CSM 11.8%.	Randomisation – concealed envelopes.	VM 40mmHg done for 30 seconds, no position specified for the VM, no clear control,.
Walker (35)	Retrospective study and prospective study	19	Standard VM vs Trendelenburg manoeuvre.	Retrospective audit of treatment of SVT, with standard Trendelenburg VM introduced in a prospective study afterwards.	Retrospective - termination rate 5.3% using an unspecified VM rising to 31.7% with specified Trendelenburg VM.	Small sample size, no power calculation, no standardisation of the method of producing a VM, so although a VM was stated to be done, no actual VM was achieved due to incorrect method; teaching done between analyses could be cause of increase in reversion rate.
Smith (57)	Retrospective study	882	VM vs Verapamil, Aramine.	VM was undertaken in 24% of participants with a cardioversion rate of 27.7%.	Reasonable population size, well-conducted search.	Effectiveness of each treatment secondary outcome, primary outcome reversion rates, potential for underreporting of failed vagal manoeuvres, no VM specification, high mean age of 57.5 can reduce effectiveness of VM (range 18-98).

Table 2 Critical Appraisal of Clinical Trials in Patients Presenting with Acute Attacks of SVT

Table 3: Critical Appraisal of Clinical Trials in Patients Presenting with Acute

Name/Author	Type of Trial	No of people	Subject	Key Findings	Positive attributes	Critical Appraisal
Taylor (46)	Retrospective study	49	Reviewed management of SVT using VM or carotid sinus massage, Adenosine, Verapamil, Diltiazem.	36.7% of patients with SVT first line treatment was VM, of these 16.7% terminated. 26.5% undertook a CSM with a termination rate of 2%, 16 patients had adenosine as first line treatment, terminating 67.4%.	Clear question.	Small sample size (only 18 undertook a VM), unclear mixed results, staed two separate termination rates, type of VM not stated, or questioned, may have underreporting of failed vagal manouevre due to no speficic protocol.
Chance (58)	Case report	3	Epigastric pressure.	Epigastric pressure was shown to increase cardioversion of SVT.		Only 3 cases.
Appelboam (59)	Case report	1	Modified VM.	Modified VM terminated SVT where previous VM had		Only 1 case.

Table 3 *Critical Appraisal of Clinical Trials in Patients Presenting with Acute Attacks of SVT*

Table 4: Critical Appraisal of Trials Conducted in the Electrophysiology Lab with Induced SVT

Name/ Author	Type of Trial	No of people	Primary Outcome	Key Findings	Positive attributes	Critical Appraisal
Mehta (37)	RCT	35	VM Strain duration 15 and 30s compared to carotid sinus massage (CSM) and human dive reflex	VM 54% termination rate, CSM 22% termination rate, human dive reflex 17% termination rate.	Repeated measures trial done initially without induced SVT, then induced. Controlled for antiarrhythmic drugs, standardised supine strain.	Induced SVT and healthy volunteers, small sample size, strain only done at 35mmHg not as effective as 40mmHg, no patient characteristics, no randomisation
Wen (34)	RCT	133	VM compared to carotid sinus massage and human dive reflex	VM terminated 43%, CSM terminated 2% with human dive reflex terminating 10%. In AVRT VM terminated SVT in 53% compared to 33% with AVRNT.	Similar patient demographics.	Not the gold standard VM – 35mmHg 20 seconds. Various different endpoints, incomplete methodology, large age range 14-72yrs, no randomisation, healthy volunteers.

Table 3 Critical Appraisal of Trials Conducted in Electrophysiology Lab with Induced SVT

Clinical trials in patients presenting with acute attacks of SVT

Four randomised controlled trials (RCTs), three retrospective/observational studies and two case reports were identified that examined patients in spontaneous SVT. This section discusses the outcome of this analysis.

There have been a number of RCTs to assess the cardioversion rate of the VM. These trials have examined a variety of different modifications with varying success, discussed in theme two. In this section, these modifications will be ignored as they are discussed below. The largest RCT (REVERT) conducted on this topic found the standard VM had a conversion rate of 17%. (2) This was echoed by Lim (18%), Montemedi (14.8%) and Corbacioglu (10.7%). (55,56,3)

As a whole this evidence produced similar rates of cardioversion for the standard VM. It is the most reliable data as it was collected from patients with SVT. This indicates that the VM is an effective first line treatment for terminating SVT.

There were some limitation to these studies. Corbacioglu used a syringe to create the VM which is not the gold standard, and has been shown to create variable pressures. (5) Lim study was different to other studies as it only allowed one attempt at each vagal manoeuvre before moving to the next. Further, patients were requested to hold the VM for 30 seconds, which has the potential to reduce the effectiveness of VM due to dropping the intrathoracic pressure as they hold it. .

The three retrospective studies present findings with a larger variation of potential termination rates, and suggest that VM is more effective when performed by specifically trained clinicians than when performed by those who are less skilled. In Walker's study, the cardioversion rate rose from 5.3% (retrospectively) to 31.7% (prospectively) when the clinician was trained to deliver a Trendelenberg VM. (35) This study used relatively small number of patients (n=19 for the

retrospective arm, n=27 in the prospective arm), which reduces the validity of the results. (35) Further, the fact that this study was performed in only one site limits the generalisability of the findings.

Other studies show that if medical professionals understand how to produce a VM the cardioversion rate increases. Taylor recorded a termination rate of 16.7% which was similar to previous clinical trials but with only 37% patients presenting with SVT treated with a VM. This could account for the study's high rate of termination and reinforces the idea that more people need to understand how to produce a VM to make it effective at terminating SVT. (46) This is substantiated by Smith who assessed 212 patients showing a VM termination rate of 27.7%, with an unspecified VM and no teaching prior to the study. (57) This is a higher rate of cardioversion than seen previously in untaught participants and closer to REVERT's termination rate. This may be due to the Australian paramedics receiving more education on the VM or similar to Taylor, only those who were confident in completing a VM carried one out. This is inferred as a further 409 patients were still in SVT on arrival, most of whom had not been treated, but some may have received VMs that had failed so were not recorded, so it is hard to draw any conclusions. (57)

It is difficult to interpret these retrospective studies as patients' records document that a VM was completed, but do not always give the specifications of how it was produced. It is therefore hard to know if an appropriate VM was completed (30-50mmHg for 15-30 seconds) and it is likely that some of these VMs were not true VM strains. (60)

Despite the limitations to the studies listed above, the body of available evidence seems to indicate that VM is an effective first line treatment in the treatment of SVT.

Trials conducted in an electrophysiology lab with induced SVT

Two RCTs were conducted with patients in whom SVT was induced in the electrophysiology lab. There is potential that induced SVT (by programmed electrical stimulation) may be more susceptible to reversion by vagal manoeuvres than a patient with spontaneous SVT triggered or maintained within the myocardium. (61) However, these studies allow for greater control of variables such as: anti-arrhythmic drug levels and potential causes of onset of the SVT and duration of attack that may affect the cardioversion rate.

The Mehta study recorded a termination rate of 54% using a VM. This study shows the highest rate of termination by VM in the literature, possibly due to the greater susceptibility of cardioversion by induced SVT. (61) The VM in the study was a strain of 35mmHg for 15 seconds. Though other papers suggest 35mmHg is low for a VM, this study has shown this pressure is still effective in carrying out a VM strain. This VM also produced a greater drop in heart rate compared to the carotid sinus massage, indicating that this is key in termination of SVT. (37)

Wen's study was also carried out on participants with induced SVT but with a much larger number of participants (133 participants) than Mehta (35 participants) giving their results more weight. (34,37) The VM performed in this study is different from the standard, as it was a 20 second strain held at a pressure of 35mmHg. This is similar to Mehta, suggesting that a pressure of 35mmHg can produce an effective strain. The Wen results showed the VM terminated SVT in 53% with AVRT compared to 33% with AVRNT. (34) The average rate of cardioversion was 43%, slightly less than the Mehta rate of 54%. Thus the evidence is increasing in support of induced SVT having a termination rate of 43-53% using VM (at 35mmHg). (37,2,34) Wen's study shows how effective a VM can be in terminating SVT. Their results are substantiated by the REVERT trial, showing that this may be possible in spontaneous SVT.

The Wen study is interesting because it looks at potential explanations for the VM not terminating SVT, including patients having a lower vagal response in the

physiological testing causing a smaller reduction in RR intervals post VM than those that cardioverted. It was also shown that patients with AVRT had a greater vagal response during sinus rhythm, but we are unable to prove a causal relationship between AVRT and its higher termination rate. (34) The VM induced the most significant ($p<0.05$) vagal response in sinus rhythm and PSVT (paroxysmal supraventricular tachycardia) compared to other vagal manoeuvres (CSM, cold water to face). (34)

Both the Wen and Mehta studies were carried out on people who have previously had SVT and many who had previously undergone VMs. This may have increased their chance of cardioversion as they were familiar with the manoeuvre and therefore had a greater chance doing it correctly. These results complement previous evidence showing that the VM is an effective first line treatment for SVT. However, it also reveals a significant degree of variation between results, indicating that there is the potential to improve outcomes.

Systematic Reviews

There are lots of small literature reviews, all calling for more research. The Cochrane Review in 2015 was unable to find substantial evidence to support or refute the use of VM in SVT. (61) However, this review only looked at 3 small RCTs with 316 participants, highlighting the need for more research and hence the inability to recommend the VM. The Smith Review in 2015 was more positive suggesting current evidence supports the use of VM in SVT, but called for additional research to standardise the manoeuvre and gain a strong evidence base. (22)

A prehospital review showed there was no literature looking at using the VM out of hospital, partly due to the difficulty of carrying out a VM reliably in the prehospital environment. A retrospective study has since been carried out by the review's author, Gavin Smith. (44) It would be a major advantage for most patients to be able to terminate SVT at home and avoid a hospital visit. (3) VMs need to be used more prehospital as there is evidence to suggest the earlier a

VM is completed, the greater chance of success; this will require an evidenced based review in due course. (6) To facilitate this advancement in the prehospital environment, the VM requires adaptation to improve ease of use.

Efficacy of different modifications

This section analyses the efficacy of modifications to the VM, to assess whether alterations to the VM can improve SVT termination rates. One systematic review, four RCTs, two repeated measures trials, two retrospective/observational studies and two case reports were analysed. The extra studies identified are on healthy volunteers and are shown in table 5 with their critical appraisal and a quick overview of the study.

This section is divided into two sections

1. Modified VM
2. Previous Modifications

Table 5: Critical appraisal of trials in healthy volunteers

Name/ Author of	Type of Trial	No of people	Subject	Key Findings	Positive attributes	Critical Appraisal
Wong (8)	Repeated measures trial	65	Which manouvre creates the lowest heart rate - supine, supine with epigastric pressure, supine and leg raise, semi-recumbent, sitting VM.	Supine epigastric pressure and supine techniques had a lower heart rate post manoeuvre than the leg raise, semirecumbent and sitting position. With a difference of 2-3 bpm.	Good control in repeated measures trial, used 40mmHg into a manometer, pilot study to indicate sample size, randomised, objective clear question.	Small population, healthy participants.
Smith and Broek (18)	Repeated measures trial	72	Which manouvre creates the largest vagal tone - Supine VM, Trendelenburg, human dive reflex	Supine VM has the greatest vagal tone. No significant ($p>0.09$) difference between supine and trendelenburg	Randomisation, repeated measures.	Healthy participants.

Table 4 Critical Appraisal of Trials in Healthy Volunteers

Modified VM

In this dissertation we have defined a “modified VM” as undertaking a VM strain in the semi recumbent position but immediately at the end of the strain, patients are laid flat and have their legs raised to 45° for 15 seconds. (2) This is a relatively new concept first described by Appelboam in 2014, when the modified VM succeeded where other VMs had failed to terminate SVT. (59)

The case report was followed by an RCT (REVERT) (n=433) which determined the effectiveness of the modified VM at terminating SVT. This research showed that the modified VM had a termination rate of 43% compared to 17% (95% CI 2.3-5.8; $p<0.0001$) in the semi-recumbent position. (2) This is a large improvement that will improve patient treatment, but it has other benefits of being a low-cost intervention and having no increased side effect profile. (2) This modified VM has recently been substantiated by Corbacioglu and colleagues achieving a very similar cardioversion rate of 42.9% for the modified VM compared to the standard of 10.7 % (CI 6.8-53 p=0.007). (55) The Wheeler Review was produced after the REVERT trial and showed that the modified VM had a greater effect than semi recumbent position in SVT; though the fact that it relied heavily on the REVERT findings for its review reduces its contribution to our knowledge on this topic. (62) The REVERT trial itself provides robust evidence for the effectiveness of the modified VM, given its high patient number, strict protocol, and highly significant findings.

These studies appear to show that the modified VM, as described previously, is significantly more likely to terminate SVT than the standard version. This has implications for patient care, as a more patients could be successfully treated in this way and thus avoid pharmaceutical management and the adverse events this is associated with.

Previous modifications

Previously various postural modifications have been studied, which include semi-recumbent, upright, standing, Trendelenburg (head down position) and epigastric

pressure (abdominal pressure in supine position). These are discussed below. REVERT also showed that the more upright you sit, the less effective your VM will be in terminating SVT, as a semi-recumbent position produced a termination rate of 17% whereas a sitting upright showed a termination of only 10.7% . (55,2,3) A similar termination rate is shown by Lim of 18%. (3) However the position of the VM is not specified, yet from the picture they provide we can guess it was in the semi recumbent position which agrees with other evidence.

No study has compared the modified VM to the gold standard supine manoeuvre. In Montamedi's recent study, he showed that the supine manoeuvre was only effective in 14.8% of patients which is lower than the semi recumbent controls of the REVERT trial. (56,2) However Mehta showed that the supine manoeuvre was superior to the standing VM in terminating SVT in 54% compared to 20%. (37)

The Trendelenberg manoeuvre was shown to be effective in terminating SVT in a case study which was then followed by two different studies. The initial study done by Walker and Cuttings showed that the Trendelenburg manoeuvre terminated SVT in 31.7%. The rate of successful cardioversion post-teaching and implementation of the Trendelenburg VM increased cardioversion rates from 5.3% to 31.7%. (35) There was no standardised method of producing a VM prior to implementation of the Trendelenburg VM, meaning that though a VM was recorded, a VM might not have been achieved due to incorrect procedure; this might account for differences in cardioversion rates compared to the REVERT control group (17% compared to 5.3%). (35,59) It is unknown whether the improvement post-teaching is due to the education or due to the Trendelenburg position as extant literature reports emergency physicians perform very poor VMs. (35,60) This is an inadequate study and it is impossible to draw any conclusions due to its flawed methodology and confounding factors stated above. The second study completed in 2014 on healthy volunteers showed the bradycardic effect of the Trendelenburg manoeuvre was not shown to be significantly different to the supine VM, which is easier to produce. (18) This shows that the Trendelenburg VM is unlikely to be superior to the supine VM.

Studies done on healthy volunteers showed there was no significant change of drop in heart rate between the supine VM and the Trendelenburg ($p>0.9$), which supports the finding that there is no advantage provided by the Trendelenburg manoeuvre. (18) Wong looked at a variety of modifications on healthy volunteers and showed that the supine technique was superior to the semi recumbent, sitting position and leg raise techniques. The reduction in heart rate was measured, and a difference of 2bpm between the supine technique and the semi recumbent and leg raise techniques was found. The sitting position produces a smaller drop in heart rate compared to the supine position with a difference of 3 bpm, however this was not significant. (8). The use of epigastric pressure during a supine VM has been shown to give no significant benefit compared to the supine VM. (8)

Overall the evidence suggests that these modifications do not provide a significant benefit in the termination of SVT compared to the standard VM.

Discussion

This literature review demonstrates the utility of the VM in SVT and also the improved effects of a modified VM in clinical practice. It was difficult to compare the RCTs against each other as different methods were used. The most important difference was between the use of healthy volunteers with induced SVT and those with spontaneous SVT. Spontaneous (i.e. non-induced) SVT may represent a more accurate way to assess the utility of the VM, as induced SVT's have a greater chance of resolution, both with and without intervention. (61) (37) The fact that some studies use induced SVT participants and others use spontaneous SVT participants makes a direct comparisons difficult.

Although the healthy volunteer studies were very effective and well carried out, their use is limited. Though a drop in heart rate has been shown to increase the likelihood of terminating SVT, this has not yet been proven to be a causal effect. (34) There are other potential causes of the VM not being as effective at terminating SVT, for example hemodynamic and electrophysiological

disturbances, which may affect the VM. However, as long as the autonomic system is intact and functional, the VM should have reproducible effects within SVT. (8,63) There is evidence linking the physiological effect of a drop in heart rate to a greater chance of SVT reversion. (34) This has also been shown by Mehta where the Valsalva ratio was shown to be significantly ($p<0.001$) higher in those participants who terminated their SVT than those that did not. (37) There are no studies examining the physiological effects of the modified VM. This study will therefore contribute to the evidence base for this treatment option.

While no direct comparisons have been made between the supine VM (40mgHg, 15s), which is the current gold standard, and the modified VM, the body of data available seems to suggest that the modified VM may be superior in terminating SVT.

Conclusion

Results from existing studies are hard to compare because of the differences in their methodology and especially differences within the technique of VM. This review shows that the VM is successful at terminating SVT and identifies the modified VM as the most effective method of VM. However, there is currently no evidence comparing the modification against the gold standard of supine VM. This study aims to address this issue.

Two – Effectiveness of strain creation

Currently the VM is created using various methods, with the gold standard being the manometer. (2,18) The second most widely used and recommended for paramedics is the use of syringes. (64). However there is mixed evidence as to which is the most effective way to produce the VM to increase the efficacy of the VM. We have divided the review into four sections to examine each method. The objective of this review is to ascertain whether a device that aids in the delivery of a successful VM, and that can be used in the pre-hospital environment, would be of value in improving outcomes for patients presenting with SVT.

1. Manometer
2. Syringes
3. Other methods of producing a VM
4. Medical professional ability to perform a VM

Manometer

Manometers have been used since the 1920s to reduce the risks of doing an VM against a closed glottis. (22) In previous studies blowing into a manometer with a specified air leak was used as the standard for creating and measuring the appropriate intrathoracic pressure. (18) This is because it's easy to measure the intrathoracic pressure this way. The manometer has been used in many large trials including the REVERT trial where it showed a cardioversion rate of the semi recumbent VM of 17% which is higher than that of the Corbacioglu study which, using syringes, showed only 10.7% cardioversion of supine VM. Potentially this shows that the manometer performed better than the syringe. However this difference is not clear because the modified group in the REVERT trial had a conversion rate of 43.5% compared to 42.9% in the Corbacioglu study. (2,55) The majority of studies have used manometers to record the pressures reached in the thorax while measuring the performance of the VM. This is due to the stability of pressure the manometer provides to make the VM as effective as possible. (2,55,37,34,3,30,45,18) There are currently no studies anlysing the efficacy of the manometer technique compared with the syringe technique in terminating SVT. We can conclude from studies done on syringes that pressures exhibited by syringes are not as exact as the manometer. (20) Thus the use of a manometer is preferable to reduce side effects and improve chances of a successful cardioversion. (22,65)

The main limitation of the manometer is its size, being very bulky and not easy to set up in an emergency situation. Vagal manoeuvres are much more effective when performed before the adrenergic tone rises so often work better at home than in the emergency room, particularly because there is often a long time between the start of SVT until treatment in the emergency room. (6) Therefore either ambulance crew or patients themselves need to be able to perform the procedure. This is why a device that is easily accessible, accurate and reliable is needed. Manometers are also becoming less available as they are being replaced by electrical blood pressure machines. However the latest study (REVERT) used a manometer with no air leak, and it did not seem to affect the effectiveness of the VM, so this is what I will use as my gold standard. (2)

Syringes

Several trials have looked into the efficacy of using syringes to perform the VM. (66) These trials are hugely variable and recommend different syringe types and sizes, indicating that the methods involved are inaccurate or the syringes themselves are variable.

The Smith and Boyle study suggests that only a 10ml syringe is useful as no other size creates the correct pressure, but the limitations of this study are manifold. (67) Firstly, only ten syringes in each size group are tested, secondly it is unclear what pressure has been recorded – the lowest initial pressure or the lowest pressure needed to move the syringe in the next 15 seconds. This means that the pressures could be hugely variable. (67,5)

The Thornton study had a different method, whereas in the Smith trial they had a patient blow and recorded the movement of the syringe, this study used a slow incremental increase in pressure by a manometer and recorded when the syringe moved, the plunger was then moved manually to 4 different positions each time checking the pressure required to move the plunger in its new position. (67)This will give a more accurate idea of what pressure is required, but it is not very

representative of the how a breath works although it is more accurate than the Smith paper. (67,5) Thornton study assessed 20 syringes in each size to assess the effect. Although this is an improvement on the Smith study it is still a very small number. This study showed that syringes are not an accurate way to reproduce the VM and could potentially produce serious side effects as 20% of syringes required greater pressures than the 40mmHg to move the plunger. (5) The range of pressures was approximately 30-160mmHg; creating pressures this high can have very severe consequences. There were no side effects recorded as this study was done using a manometer not a patient. These results are limited as only one brand of syringe was assessed and not by a randomised controlled trial on patients in SVT. Their poor performance can be applied across syringes which are not manufactured or designed for this purpose and thus lack quality assurance on achieving the right pressures, there is potential for other brands of syringe to create higher pressures. (5)

Syringes have other limitations as well; a constant air leak is required to prevent supraglottic pressure requiring constant movement of the plunger during VM. However, this is problematic due to syringe size and the variation of gliding force along the syringe. (66) These trials demonstrated that all syringes had very high pressures if the plunger had not been previously moved. (5) The pressures also vary with movement of the plunger due to static friction which increases with time. This means if the plunger is moved to reduce the initial high pressure, we are unable to ensure the friction will be the same throughout the syringe, which in turns means that the required maintenance pressure of 40mmHg cannot be reliably achieved. (66)

The current NICE guidance is to do a VM, and the example given on how to perform this manoeuvre is: blow into a syringe for 15 seconds lying down (supine). (17) This guidance may have been based on the evidence of Gavin Smith's paper in which he did a very small unblinded study that showed that 8 of the 10ml Terumo syringes examined created pressures of between 30 and 50. (67) The international standard is to create a pressure of 40mmHg to achieve the maximal vagal response and that a pressure above 50 mmHg is the dangerous

limit. The Smith and Boyle study conforms to this. (67) However, as this would have to be recreated on a much larger scale to be a significant result, there needs to be a randomised controlled trial assessing the VM efficacy with the syringe against the manometer.

Other ways of producing a VM

There are several other ways of producing a VM; blowing against a closed glottis, straining like a defecation and creating an abdominal pressure. (65) Though not all of these create a true VM they are often used in practice due to the lack of available equipment to do a formal VM. These methods have not been tested, according to the literature, but as studies show that specific pressures are required to produce an effective VM. (30) We can say that these methods are almost useless due to the very variable pressures they create.

Medical professionals' ability to produce a VM

Research findings show that doctors' knowledge of the VM is poor and this is hindering patients' treatment as VM is either being performed incorrectly or bypassed. (46) As shown in the Smith study where, of the 882 patients admitted with SVT, the VM was only undertaken in 212 patients, it is often neglected in favour of drugs. (57) Lim also discovered that 12.2% of VMs were performed inadequately. (3) There have been four further papers examining this.

Taylor and Wong showed that 91.4% of registrars and emergency medicine physicians performed a VM in an incorrect position with the majority placing people in an upright position greatly reducing the chance of successful cardioversion. This study showed how poorly VM is currently understood and used in most emergency departments. (60)

The Honarbakhsh study showed that only 1/28 patients terminated their SVT with a VM, which shows an abnormally low conversion rate of 3.6% for the VM which may be due to incorrect methods. (68) One possible explanation for this is the

lack of clarity surrounding the use of the term “vagal manoeuvre”. It was not made clear whether this referred specifically to the valsalva manoeuvre, or to other vagal manoeuvres such as carotid sinus massage. This may have resulted in the abnormally low reversion rate. As this was also not a stated endpoint of the trial it is hard to draw any conclusions from this data.

Smith and Boyle’s study showed that only 1/46 (2.2%) paramedics carried out the correct method of VM, with 34.8% getting patients to blow as long as possible. A VM is then very unlikely to take place as the correct pressure within the chest would not be created due to reduced lung capacity. (65) This was a cross-sectional study with face-to-face interviews with paramedics who were asked how to perform the VM on a patient with hemodynamically stable SVT, while being blinded to the research question. This study gives a useful insight into the beliefs of paramedics around their own practice, and by ensuing the participants were blinded to the research question, the validity of the study is increased. However, the use of self-reported VM techniques, as opposed to directly observed real-world or simulated practice, draws into question the validity of the findings, and could overestimate the paramedics’ ability to deliver an effective VM.

One of the most compelling pieces of evidence is the Walker and Cutting study showing that with education and a standardised manoeuvre the cardioversion rate increased from 5.3% to 31.7%. (35) There was inadequate detail in patient records of how the VM was performed so a questionnaire was completed by a cross-section of 32 medical staff. This showed only 20% placed patients in a supine position, with the mean strain duration being 10 seconds, 13% asking patients to blow for long as possible. It was also shown that no one used a manometer and 93% used a syringe without the size specified. This suggests that very few true VMs performed due to a lack of knowledge. Doctors tend to overlook the VM, for many reasons such as lack of standardisation of techniques, lack of appropriate equipment, fears of the risk of harm (a remnant from carotid sinus massage), previous failure and ease of using Adenosine. (46,60,68,69) Other factors impacting the use of the VM include poor education and instruction, therefore a small and easy to use device will increase the use of VMs. (60) This

shows the benefit of having a standardised, recognised VM which is simple to administer, has the potential to increase the correct use of VMs.

Conclusion

The literature suggests that current methods of producing a VM strain are inadequate in the pre hospital environment. The manometer was shown to be easy to use and can accurately produce a VM in the emergency department; however, it was too bulky for the prehospital environment. The literature also implies the need for a simple standardised method for the VM to improve correct completion by medical professionals improving its efficacy and use.

A new portable device with instructions for a standardised VM is very much needed to utilise the pre hospital environment because the earlier the intervention the better the clinical outcomes. (65,6) It would also improve the delivery of the VM in the emergency department.

Complications of VM

In designing a study using healthy volunteers it is important to be aware of the potential harmful effects of the VM. Any adverse reactions are very rare, and the VM is commonly accepted as a very safe procedure. (20) Complications of this manoeuvre are more likely to be seen if the VM is done with too high a pressure. (22) As this would exaggerate physiological effects, mostly due to reduced venous return causing significant increased hypotension, increase in venous pressure and changes in the cerebral blood flow. (70) The exaggerated cardiovascular reflexes have been associated with increased morbidity and even mortality. (28) It has been shown in previous studies that pressure of 40mmHg for 15 seconds is a safe manoeuvre to carry out and if it rises above 50 mmHg, there is a higher risk of retinal haemorrhage or stroke. (22,20,37)

However some serious side effects can occur in patients, these include chest pain, syncope (greatly increased with aortic stenosis), arrhythmia or stroke. (71) These risks are generally very low but are increased in patients with coronary artery disease (CAD) or cerebrovascular disease. (20) In patients with CAD where myocardial blood supply is reduced, ischemia can be precipitated by reduced venous return causing hypotension which increases the myocardial oxygen demand caused by high blood pressure after the strain. (28) The VM can also trigger arrhythmias, e.g. non-sustained tachycardia, conduction block and atrial fibrillation. This is thought to be due to changes in vagal tone and cardiac repolarisation being altered by ventricular loading. (28) Very rarely more severe consequences are seen, for example, due to the reduction of the left ventricular stroke volume during the manoeuvre complicated by inefficient autonomic regulation, it may contribute to a cardiac arrest. (20) Other complications can occur in the eyes, brain and lungs.

The ocular complications are caused by a rise in intraocular pressure, which can trigger a retinal, macular haemorrhage (previously called Valsalva retinopathy or maculopathy) or glaucoma. (20,72)

Significant decreases in cerebral perfusion have been demonstrated during the strain phase, making the feeling of dizziness and fainting the most common side effect. (28) It has been implicated that this drop in perfusion followed by the rapid increase in blood flow can cause cerebral aneurysm rupture, though this is very rare. (28) The lungs can be damaged due to reducing pulmonary venous flow; decreased mucosal blood flow and size of upper airways, the most important consequence is barotrauma which can cause alveolar rupture leading to pneumothorax, subcutaneous emphysema, pneumomediastinum. (71) However, this risk is greatly increased with the concomitant use of drugs, e.g. marijuana and cocaine. (28)

The majority of these cases are recorded as case reports due to the rareness of these side effects, however in this study, it is imperative that we do not put people at risk, so, we are excluding all patients with any eye, heart or lung disease, blood pressure of less than 100mmHg, pregnancy or any regular medications (excluding the oral contraceptive). These side effects are very rare-in a study of 20,000 people no one experienced any complications. (20) Other more common side effects occur, which are much less serious for example: headaches, dizziness, musculoskeletal pain, nausea or altered vision, the most common of which was light-headedness and occasional premature ventricular ectopic beats. In a study of 65, these side effects only occurred in a few patients. (8,20) In the REVERT trial out of 428 patients only 21 patients had minor adverse events. These adverse effects were slightly increased in the modified VM group compared to standard manoeuvre. (2)

Studies suggest that pressures above 50mmHg are likely to result in side-effects such as retinal haemorrhage or glaucoma but the use of 40mmHg as a safe pressure is supported by good evidence. (22)

Chapter Three - Valsalva Assist Device

To improve the VM results the device needs to be small, portable, accurate, safe and easy to use. It has been shown that previous methods of blowing into syringes are very unreliable and can be unsafe due to high pressures created. (66,28)

The benefit of this device is its user friendly design with simple instructions for performing a correct VM. This will be instrumental in introducing a standardised, easily reproduced VM. Introduction of the VAD is also a teaching opportunity to improve the effectiveness of the manoeuvre in emergency and pre hospital environments. (62)

VAD development

The initial idea was to develop a new small portable device which would enable patients to carry out their own VM safely and efficiently. Although a manometer was an accurate and reliable way to provide VM strains in trials, it has a number of problems for routine use, the first being its size, preventing ambulances from carrying them. The second problem is the creation of a small seal around a tube to create the appropriate pressure, as observed in ED some people are incapable of achieving this.

Figure 6 Original Device

Novel design solutions for such a device were considered, however the investment required to produce these, such as new injection moulding equipment would have made the supply of devices for study prohibitively expensive. So we tried an alternative route using the company Meditech who make parts for airlines and anaesthetic circuits. Meditech utilised parts that were already available to create the initial device (shown in figure 6). It worked by employing an ALP valve, similar to anaesthetic circuits, which pops open at 40mmHg. During pilot and preparation work for this study, we found a potential problem with the proposed VAD. The air leak was too great for some participants to complete the VM as described by blowing for the full 15 seconds. Whilst not dangerous, this would reduce the efficacy of the manoeuvre and be likely to confound the results of the study. The air leak is very important as it creates the correct intrathoracic pressure by opening the glottis.

.

Figure 7 Original Device with Filter

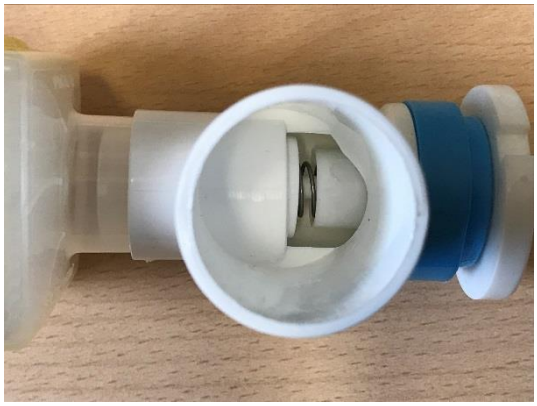

Figure 8 Valve in VAD

Initially, we tried to reduce this air leak by applying a cap, as shown in figure 9. However, this was unsuccessful.

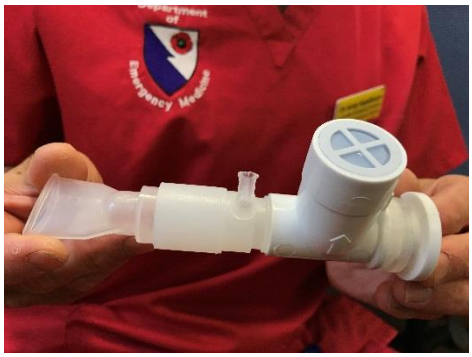

Figure 9 Second Iteration of VAD with Pressure Measuring Attachment

We then had to design a new device with a smaller air leak. We worked with the manufacturer towards a solution whilst still using a device that is CE marked and fit for purpose. This led to a period of innovation which involved Mr Clowrey

(Meditech managing director), Mr Mcleod (innovation lead at RD&E) and I visiting the Meditech factory. We tried a variety of techniques to improve the device using the same valve system so when the valve was triggered either sounds or a visual stimuli would be produced while also reducing the air leak shown in figures 10-14. Unfortunately, none of these created the correct pressure reliably, and all the sound producing ones were too hard to hold for the full 15 seconds.

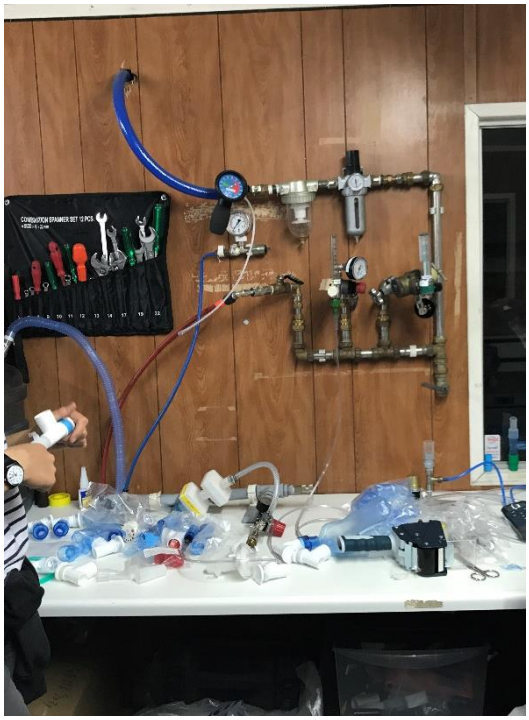

Figure 10 Designing Station and Calibration

We also found why the initial device had passed its industrial screening but failed on people. We had been testing the devices using air pressure with a volume of 35 litres per minute which is not feasible by a human who has a maximum lung capacity of 5 litres and a tidal volume of 500ml.

Figure 11 Attempts at Making Device Make Sound at the Correct Pressure

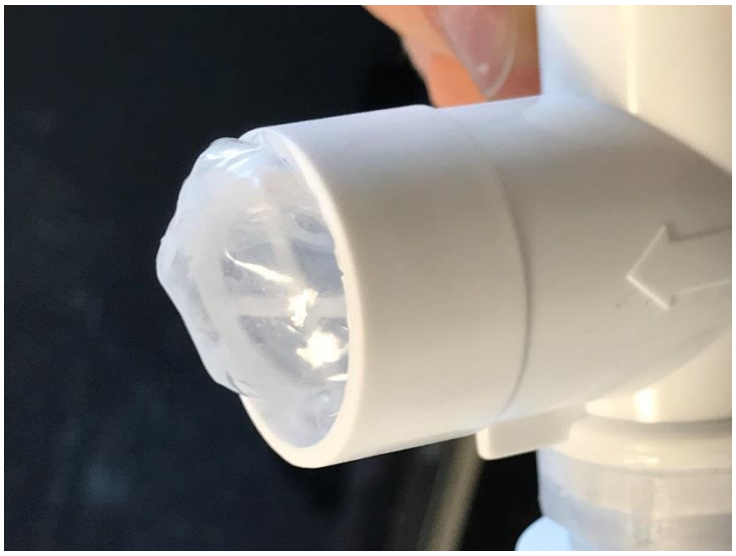

Figure 12 Attempts at Making Device Make Sound at the Correct Pressure

Figure 13 Attempts at Making Device Make Sound at the Correct Pressure

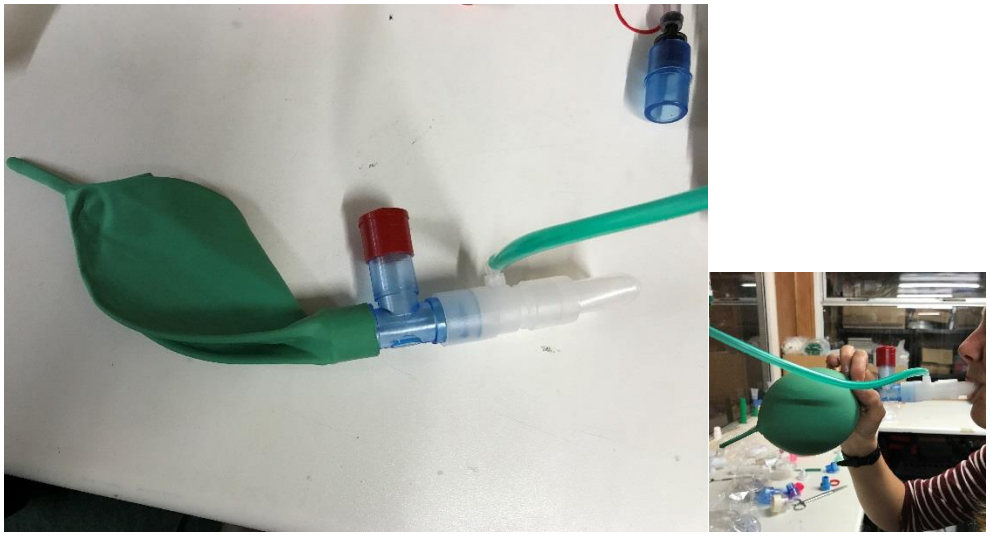

Figure 14 Attempts at Making Device Make Sound at the Correct Pressure

After trial and development, we found a sample manometer that we could use. This turned out to be the most effective way to achieve a constant pressure

accurately so we added this to our mouthpiece to create our VAD as shown in figure 15.

This device has several benefits including an actual manometer (pressure gauge), so the patient can see how high the pressure is. This new VAD will improve the standardisation and quality of the strain and reduce the chance of blowing at too high a pressure. We believe this VAD to be superior in design and closer to achieving our goal, an easy to use alternative device to a manometer. We ensured we have the best VAD to test so the study delivers its objectives but is controlled and safe.

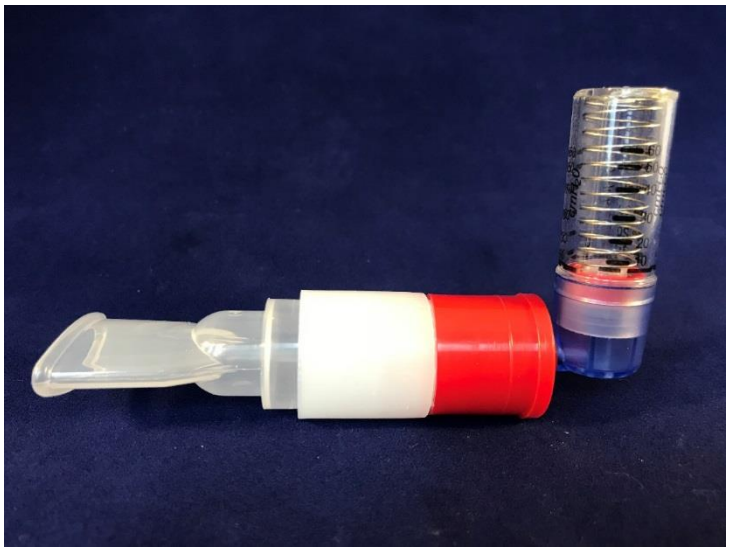

Figure 15 The Final VAD

This design has been given registered design status.

Rationale

The rationale behind this study is the need to provide an easy and accurate way of reproducing the VM and making it as effective as possible in the prehospital and emergency settings. The aim is to reduce the need for many hospital admissions, and give patients greater control over their conditions by using the device themselves, allowing them to terminate their SVT without the need for admission.

The primary outcome of this study is to assess the effectiveness of the Valsalva assist device in reducing the heart rate of healthy volunteers, as this is correlated to successful cardioversion in SVT.

The modified technique has already been shown to be superior in terminating SVT compared with the standard technique. (2) This study will compare the modified VM with the supine VM, which has not been examined before as a secondary outcome.

Hypothesis

The VAD will have a greater efficacy than the manometer at creating a VM in the supine and modified VM positions.

The modified VM will cause a greater drop in heart rate (increased vagal tone) compared to the supine VM with both the manometer and VAD.

Chapter Four – Methods

The trial was approved by the University of Exeter ethics committee and registered with ClinicalTrials.gov (NCT03298880). We performed a randomised repeated measures trial in the Clinical Research Facility between November 1, 2017, and February 5, 2018.

Power of study

Sample size calculations were based on a simple paired t-test and the creation of a superiority study. There was no obvious way to determine the "smallest clinically important difference", but we have used 4 beats per minute as a reasonably small difference, below which is unlikely to be important clinically. (18) With these parameters, a sample size of at least 73 participants provides 80% power at the 5% level of significance. We increased this to 75 to allow for any missing data in results.

Participant selection and recruitment

This study recruited 75 healthy volunteers, employing convenience sampling to recruit participants. They were recruited using posters and social media posts placed in the University of Exeter Medical School and the Royal Devon and Exeter Hospital. The majority of participants were current students at the University of Exeter. Potential volunteers sent us an email stating their interest in participating. Participant information was given out at least 24 hours prior to volunteers participating, so they had enough time to read and understand the trial and what they would be undertaking. Written informed consent was obtained by me prior to participation in the trial.

To get the approval of the University of Exeter Ethics Committee we had to make sure our VAD was appropriately CE marked. The study was also approved by the Royal Devon and Exeter Hospital, so we could use their facilities. Two subsequent ethical amendments were made, the first to change the VAD we were using and the second to improve recruitment by using social media.

The inclusion and exclusion criteria are shown below. Participants were screened using a questionnaire to ensure they were healthy prior to their participation (shown in appendix D). This was self-reported, and no follow up was done. This was done to ensure the safety of the participants and to keep participants as similar as possible. We excluded pregnant women as they had an increased risk of fainting due to the reduction in venous return already impaired by pregnancy. We also recorded some demographic and health-related data on participants to enable possible post hoc analysis such as sex, age, and smoking status.

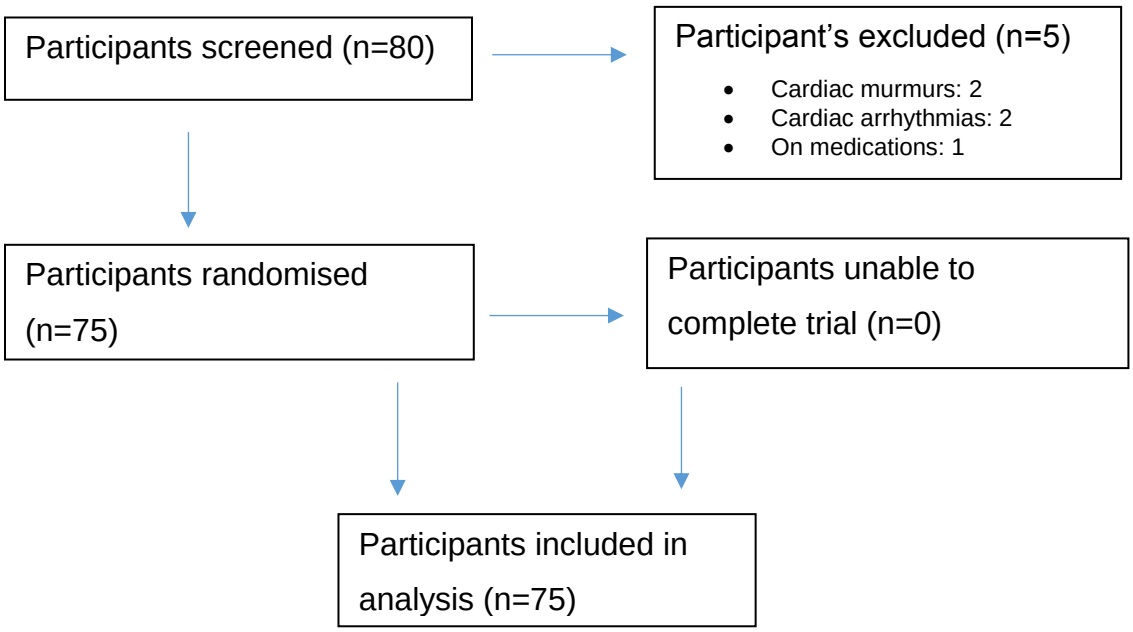

Table 5 Participant Recruitment

Inclusion and exclusion criteria

Inclusion Criteria
Adult volunteers 18-60 year-olds
Sinus rhythm on initial ECG
Self-reported good health
Exclusion criteria
Any regular medication other than the oral contraceptive
Previous cardiovascular or respiratory disease
Any contraindication to performing a VM (e.g. known aortic stenosis, recent myocardial infarction, glaucoma, retinopathy)
Pregnancy
Any ECG abnormality
Any contra-indication to postural modification (any reason the participant can't lie flat and have both legs lifted to 45 degrees, e.g. prosthetic hip
Inability or refusal to give written consent to take part.
Observations of the pulse, oxygen saturations, respiratory rate or blood pressure outside the normal range. Specifically blood pressure less than 100 systolic
Caffeinated drinks within 6 hours prior to testing
The use of stimulant drugs or alcohol within 24 hours prior to testing

Table 6 Inclusion and Exclusion Criteria

Our method was based on previous studies using healthy volunteers and trying to reduce bias as much as possible. (8,18) We used similar inclusion and exclusion criteria to previous studies and did our own literature review (chapter two) to rule out any possible risks to the safety of our participants. We excluded participants who had had caffeinated drinks within the last 6 hours as this would reduce their response to the VM. Though obesity would also reduce the response to the VM, it is a much smaller reduction, so we did not exclude these participants as this may have hindered our recruitment and ethics approval. As age affected the VM response, we have excluded participants older than 60 years. Participants taking recreational drugs have a much higher chance of adverse events, so were also excluded.

Research design

After screening I conducted some general observations to check each participant's health. Their heart rate, respiratory rate, oxygen saturation and blood pressure were recorded prior to starting the manoeuvres using a vital signs monitor (Dinamap V100). Participants also underwent a respiratory and cardiac examination by me, to ensure that the basic examination was normal. A 12 lead ECG was then carried out (MAC 1200 ST) and reviewed by me. If all of the above were normal, then participants continued in the trial.

Testing was conducted indoors with a mean ambient room temperature of 22 degrees. Each participant underwent four VMs of the four variations shown below.

1. **Supine VM using manometer**. Supine Valsalva strain using a manometer visible to the participant with a target of 40mmHg for 15 seconds.
2. **Supine VM using VAD**. Supine Valsalva strain using the VAD connected to manometer invisible to the participant but visible to a researcher for 15 seconds.
3. **Modified *VM using manometer***. Participant at 45 degrees, Valsalva strain using a manometer visible to the participant with a target of 40mmHg for 15 seconds followed by supine positioning and passive 45 degree leg lift immediately at the end of the strain for a further 15 seconds (modified VM).
4. **Modified VM using VAD**. Participant at 45 degrees Valsalva strain using the VAD connected to manometer invisible to the participant but visible to a researcher for 15 seconds followed by supine positioning and passive 45 degree leg lift immediately at the end of the strain for a further 15 seconds (modified VM).

Each participant received spoken instructions on how the study would be carried out. These instructions are found in appendix D. Participants were allocated to their order of VMs and their participant number using pre-randomised sealed envelopes. The order of VM was previously randomised and stratified to create the same number of the different orders of VM. This was done by listing all the

possible orderings and then used a random number generator to determine the ordering. This was repeated three times and then the last few were completely randomised. Each time a VM was carried out the randomisation form was signed by an independent researcher who was not a part of the research team. This was to remove the possibility of completing an order different to the one specified by the randomisation. Then the three-lead ECGs were attached and tested to ensure they were attached correctly. In this study, everything was explained to make the participant aware and to reduce anxiety. After correct positioning, participants were given five minutes of rest time to enable them to return to their baseline heart rate. The trace was started 15 seconds before the VM.

The strains are intuitive with feedback from the manometer or VAD, and no practices were allowed. A laptop stopwatch was used to time strains and was visible to participants. Participants were instructed to stop blowing after the 15 second strain, but no other encouragement or instruction was allowed. The ECG trace was stopped 15 seconds after the end of the VM. We chose 15 seconds for the strain as the available evidence suggests this is the best method and the majority of the evidence used 15 seconds, so we would have a similar risk of adverse effects. The 15 second strain also enables greater compliance to the manoeuvre than longer strains. (18,60) We tried to ensure that all participants completed the 15-second strain. However, we were concerned that significant air leaks in the Valsalva assist device might make this problematic and could affect the trial.

No participant was allowed to blow more than 50mmHg on either the manometer or VAD, due to the increased risk of side effects being caused above 50mmHg. In the unlikely event of VAD malfunction (i.e. it provided no resistance or resistance was greater than 50mmHg), the VM would have been immediately abandoned, and the malfunction recorded as an adverse incident. The manoeuvre would then be restarted using a new VAD if the participant was happy to continue.

All testing was performed on a standard hospital trolley in the clinical research facility with a manually adjustable backrest. A 45-degree-angle template was used to ensure consistent leg elevation angle where needed. A protractor was used to measure and create a back angle of 45 degrees for each modified VM.

Each participant was asked to take enough breath to complete the manoeuvre before blowing into the VAD or manometer. This was done to try and remove the size of breath intake as a factor affecting the response of the VM. This was explained to each participant at the outset. We know it is crucial to have an air leak while performing a VM to ensure an open glottis and correct intrathoracic pressures. However in ED where the manometer is most commonly used there is no easy or standardised way to create a leak in the circuit. Therefore this is very rarely done. We replicated this in our study and did not add an air leak to our oxygen tubing.

A new VAD and a new 92cm length of green oxygen bubble tubing for the manometer (Welch Allyn Maxi Stabil 3 A grade) was used for each participant. The tubing was 92cm to ensure the diameter of the tubing was the same and long enough to reach the participant, due to the bubble tubing changing diameter with length. The tubing was replaced with each participant for hygiene reasons but it was unnecessary to replace the manometer, since it has no appreciable flow of air across it. How quickly the participant was able to reach the appropriate pressure and fall at the end may be very important for the heart rate response. To rule this out as an effect, we ensured that participants achieved appropriate pressure levels as soon as possible (included in standard instructions).

There was a three-minute washout period between strains including two minutes rest after any change in posture. A continuous three-lead ECG monitoring on a standard print (running at 25mm/second via defibrillator (Heartstream XL defibrillator) was used to assess heart rate during the manoeuvre. An ECG rhythm strip trace was printed for 45 seconds (15 seconds before, during and 15

seconds after each VM). Points were marked at the onset of each Valsalva strain, labelled with a code and subsequently analysed, blind to technique according to the method described by G Smith. (18) ECGs were marked with each participant's number to enable the investigator to be blinded at a later date.

Pre-manoeuvre heart rates were determined by calculating the mean R-R interval of the 10 beats preceding each manoeuvre before converting it to heart rate in beats per minute (bpm). The lowest post manoeuvre heat rate was determined by measuring and recording the longest R-R interval during, and up to 15 seconds post, manoeuvre. This was also converted to a heart rate in beats per minute. The difference between the pre- and post-manoeuvre heart rate was taken to indicate the degree of vagal tone or slowing of heart rate induced by each manoeuvre. This was calculated as the post VM value minus the pre VM value, in seconds. (18) Intervals, where a premature ectopic complex resulted in a compensatory pause, were excluded from the pre-manoeuvre R-R interval measurement. Non-differential measurement bias is likely to have affected the accuracy of results because R-R interval measurement directly from an ECG strip is inherently inaccurate. To minimize this inaccuracy, blinding of the investigator who undertook ECG measurements was instigated to minimize observer bias and then repeated by a different blinded investigator who was not a member of the research team. (8) The Valsalva ratio was calculated by dividing the pre manoeuvre heart rate by the post manoeuvre heart rate.

Peak sustained pressures achieved as observed on the manometer and duration of longest strain attempt during all VMs were recorded on a standard report card to allow comparison of the different strain techniques. Participants were closely monitored for any adverse events. No major side effects were experienced; any participant that felt unwell or developed any significant or persistent ECG abnormalities, were immediately withdrawn from further testing, and appropriate further clinical assessment arranged. All adverse events were recorded, graded and reported immediately to the CI and University of Exeter and reviewed by the study team.

Statistical analysis

The study aims were to measure the mean difference in RR interval and mean difference in heart rate values pre- and post-manoeuvre; these were calculated from each type of manoeuvre and compared. The mean difference between the different types of VM was also compared. The two end comparisons we assessed were:

1. Supine VM vs modified VM (recognising that this comparison may or may not be different according to which instrument is used – manometer or VAD)
2. Manometer vs VAD (recognising that this comparison may or may not be different according to the posture adopted – supine or modified)

The analysis was based on mixed-effects linear regression (with an appropriate assessment of assumptions, e.g. normality), with the individual as a random effect, position (supine/modified) as a fixed effect, and instrument (manometer/VAD) as a fixed effect. An interaction term (position and/or instrument) was examined to consider whether there was any evidence of a differential effect (of the device according to the position, or equivalently position according to the device), but was dropped from the model if $p>0.1$. The interaction term was dropped so the two comparisons were presented overall. The statistical analysis was undertaken using STATA and Excel software.

Reducing bias

A standardised set of instructions for the procedure was created and printed out (see in Appendix D). This was to ensure that all participants received the same instructions, to rule out any potential instructional bias.

A mixed linear regression analysis was carried out, to assess whether or not the manometer or VAD affected the analysis of the supine vs modified VM and vice versa.

Data collection

The screening data was kept with each participant file. The ECGs were kept with the VM data sheets for subsequent analysis and were stored securely in the Clinical Research Facility.

Strain pressures analysis

35mmHg to 45mmHg was chosen as the limits of an acceptable pressure as the lower limit has been shown to be just effective if not more effective than 40mmHg. (37) This made it reasonable to assume the same variance was acceptable in the upper limit.

Reflection on Challenges

Our first challenge was receiving ethics approval, this took much longer than expected with many revisions and comments from the ethics committee. The initial ethics application was submitted in June yet it was not approved until the beginning of September. It was a very enlightening experience about how ethic committees work and how precise you have to be when writing an application. You have to think through every possible outcome of your study and how you would cope with serious adverse events. At the time this felt very forced and unrealistic. However I realised how important this is during my study and how essential it is that you have thought of how deal with these things before they happen. It was reassuring to know I had these plans in place.

We trialled our study protocol, which was a very useful exercise because it exposed several methodological issues. The first being the complexities of roles and creating standard operating procedures that would work and flow. Secondly we discovered the VAD did not work as anticipated and had to improve it before we could start. Thirdly we identified how to mark and measure the ECGs.

During the study itself we faced a variety of challenges, firstly the use of a variety of assistants. We tried to reduce the number, but every new assistant we used made the first modified VM jerky even if we practised beforehand. This may have had a consequence on participants as they may have reacted to falling backwards even though they were supported.

The unfamiliarity of the VAD meant it was difficult to use as intended; often the second attempt was much better as the participant became familiar with the VAD. This often prevented participants from running out of breath the second time. Initially, participants found it difficult to read the VAD, but participants did much better after I demonstrated one.

Our main challenge was recruitment. Initially, I thought that this would be easy as we had a large cohort of medical students that would be keen to take part. However, it was much harder than I imagined to encourage people to participate. Our initial poster campaign was not as effective as hoped, so we applied for an ethics amendment to be able to advertise on social media and this proved much more effective.

Chapter Five - Results

A total of 75 healthy participants, 30 male (40%) and 45 female (60%), were recruited to this study. The mean age of participants was 26 (range 19-55 years). Table 8 shows the baseline characteristics of participants. All participants completed the study, and there were no missing data. However, there was one VAD malfunction with the pressures reaching 55 and recording only 40mmHg on the VAD. Five participants failed screening and were excluded from participating, due to participants having heart murmurs (2), arrhythmias (2) or being on medication (1). Due to such low numbers of smokers and small spread of age, we were unable to do a post hoc analysis of these effects.

	Participants
Mean age	26.19 years
Age range	19-55 years
Base HR	76 bpm
Base blood pressure	123 / 71mmHg
Smoker	5
Never smoked/former smoker	70
Oral contraception	10
Medication	2
Past Medical History	3

Table 7 Participants Characteristics

Agreement of readers

Two readers analysed the ECG strips. For the 10 beats prior to the manoeuvre, there was very good agreement: both reporting overall means of 180.8mm.

Both reported 71% of the 300 readings were identical, with 99% of readings within 1mm and the (single) worst discrepancy being 2.5mm. For the post VM, longest RR interval, the two readers recorded overall means of 27.8mm, with 80% of readings identical and 100% within 1mm. A simple average of these two readings was subsequently used in the analyses.

Modified VM compared to the supine VM

The raw data collected from every WM undertaken is shown in figure 17. This figure shows the change in heart rate was larger in the modified VM compared to the supine VM. Due to the normal distribution of data it is easier to view as a mean value. The original data is found in appendix G.

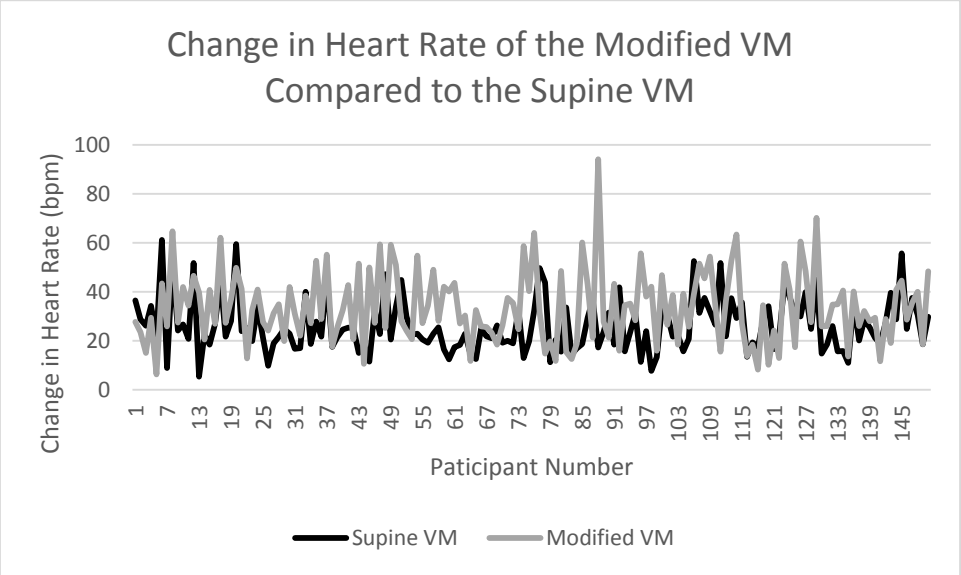

Figure 16 Comparing Raw Data: The Change of Heart Rate of the Modified VM vs Supine VM

The results are shown in table 9. Both groups showed a significant drop in heart rate following the VM, with all having a Valsalva ratio >1.3. The modified VM had a greater drop in mean heart rate than the supine VM, with a difference of 7.6 bpm.

Manoeuvre	Mean pre manoeuvre heart rate (bpm)	Mean post manoeuvre heart rate (bpm)	Mean difference heart rate (bpm)	Valsalva ratio
Modified VM	88.3	54.6	33.7	1.66
Supine VM	83.0	56.9	26.1	1.47

Table 8 Modified VM Compared to Supine VM Raw Data

However, the modified VMs pre heart rate started at a higher rate as shown in figure 18 and table 9. A mixed linear regression was completed to assess the statistical significance of these results.

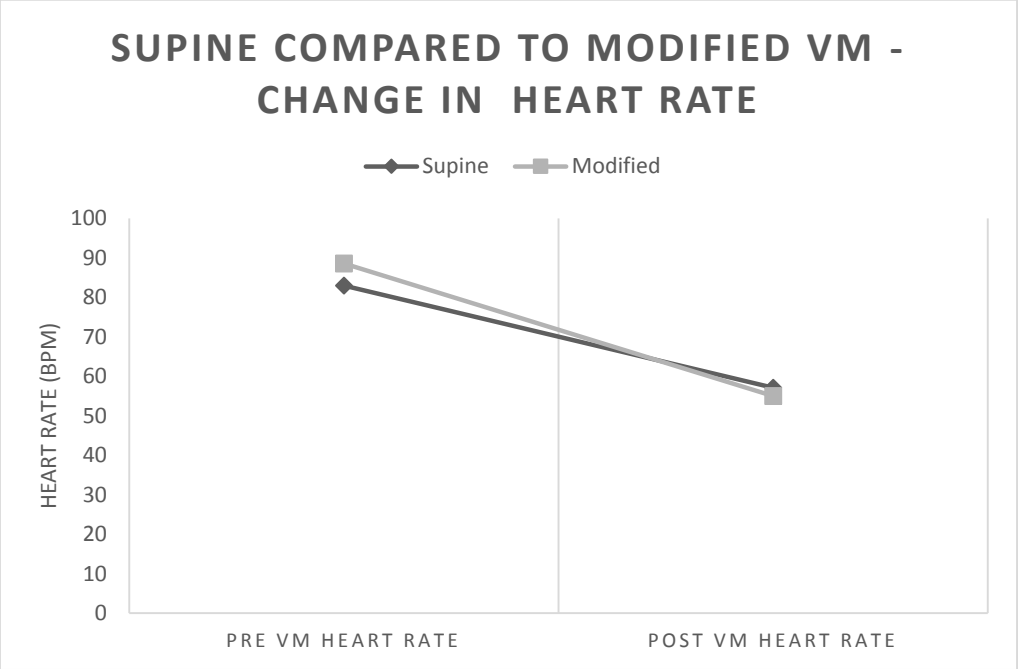

Figure 17 Change in Heart Rate of the Supine vs Modified Manoeuvre.

The coefficient was calculated for the difference in drop in heart rate (bpm) at -3.7 (95% CI 2.1 to 5.3; p<0.001). This is the statistically adjusted drop in heart rate. This was analysed for potential confounding factors (device or manometer and order of VM's) and has been adjusted allowing for baseline heart rate due to a high resting heart rate. If we remove the high pre VM heart rate as an interaction the coefficient becomes 7.7 bpm (5.6 to 9.8 p<0.001). This analysis is shown in table 10.

Manoeuvre	Significant reduction in mean difference (HR)	Confidence intervals	P value	Standard error
Modified vs supine mixed linear regression	3.8	2.2 to -5.4	P<0.001	1.12
Modified vs supine - removed the higher pre VM heart rate	7.6	5.5 to 9.7	P<0.001	1.08

Table 9 Modified VM Compared to Supine VM – Mixed Linear Regression

VAD compared to the manometer

The results of the VAD compared to the manometer are shown in table 11. Each VM showed a significant drop in heart rate following the VM, all with a Valsalva ratio >1.3. The manometer showed the greatest drop in heart rate compared to the VAD.

Manoeuvre	Mean pre manoeuvre heart rate (bpm)	Mean post manoeuvre heart rate (bpm)	Mean difference heart rate (bpm)	Valsalva ratio
Manometer	85.5	54.7	30.7	1.59
VAD	85.8	56.7	29.0	1.53

Table 10 Manometer and VAD Raw Data, Heart Rate

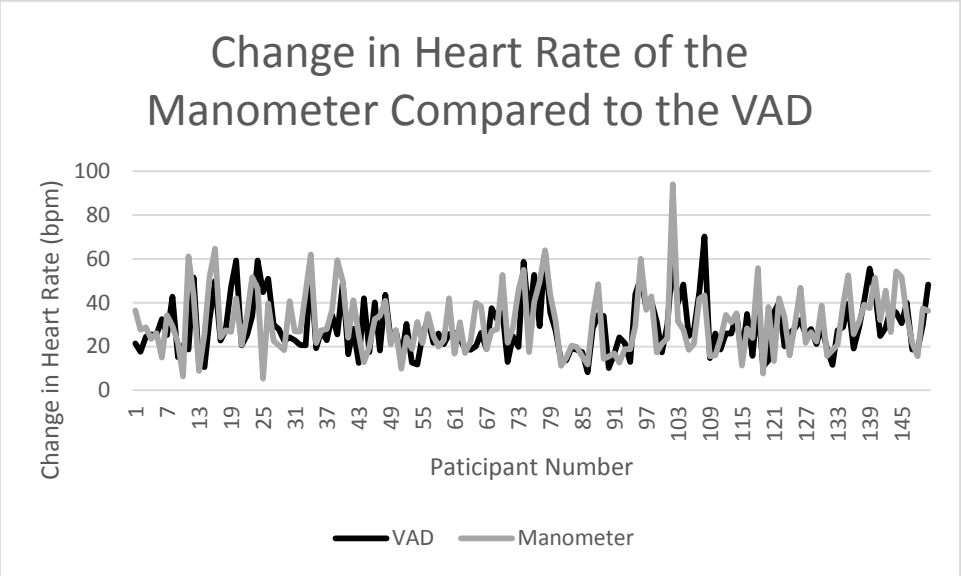

Figure 18 *Change in Heart Rate Raw Data With the Manometer vs VAD*

Figure 19 shows that the raw data appears to be very similar for the manometer and the VAD. Yet the comparison of the mean heart rate difference between the manometer and the VAD (shown in figure 20) shows a greater drop in the manometer group. The original data is found in appendix G. The difference in heart rate drop of the manometer compared to the VAD was 2.17 bpm. A mixed linear regression was completed to assess the statistical significance of these results, shown in table 12.

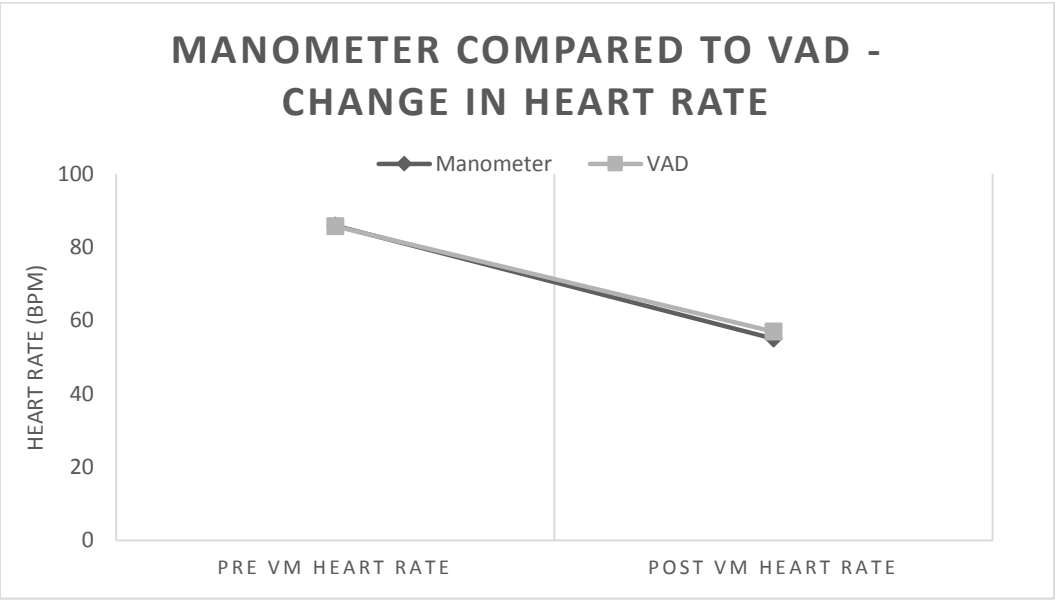

Figure 19 Comparing the Pre and Post VM Heart Rate Analysing the Manometer vs the VAD

Manoeuvre	Significant reduction in mean difference (HR)	Confidence intervals	P value	Standard error
Manometer vs VAD – mixed linear regression	1.9	0.04 to 3.4	0.01	1.09
Manometer vs VAD – removed the higher pre VM heart rate	1.7	0.4 to 3.8	0.11	1.08

Table 11 Statistical Analysis of the Manometer and VAD

Statistical analysis shows the manometer produces a greater drop in heart rate compared to the VAD, with a coefficient of 1.9 bpm (95% CI 0.4 to 3.4; p=0.01). However if we remove the high pre VM heart rate as an interaction, the coefficient becomes -2.0 bpm (95% CL -4.1 to 0.1; p=0.06).

There appears to be very little difference between the manometer and VAD, with most of the difference appearing in the supine group of the VAD group (this was shown to not be significant p>0.05).

Valsalva ratio

We assessed participants' Valsalva ratio to determine the effect of the VMs and more easily compare ours to previous studies. Figure 22 shows the spread of data for the modified VM vs the supine VM.

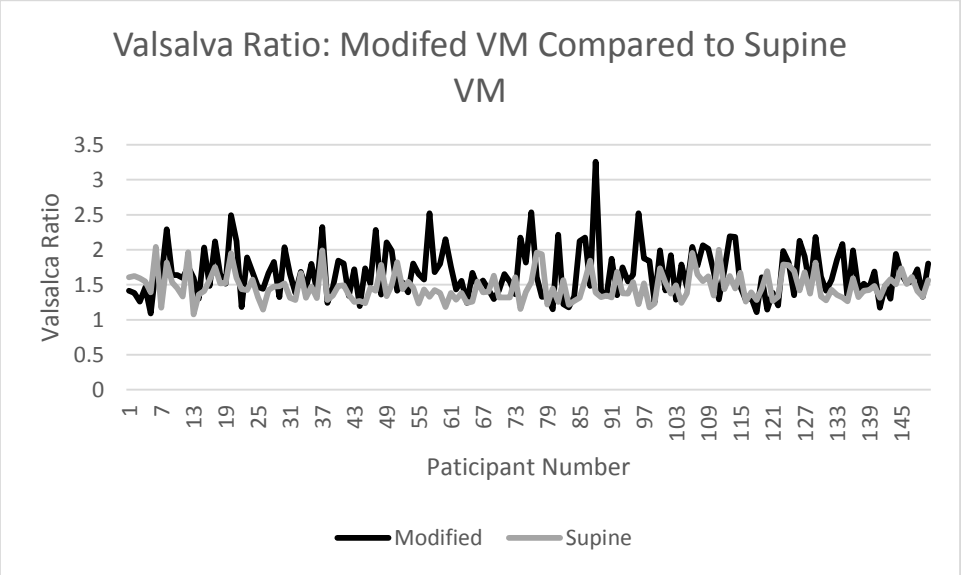

Figure 20 Valsalva Ratio Raw Data of the Modified VM vs Supine VM

From figure 22 it is evident that the modified VM has a greater Valsalva ratio than the supine VM in the majority of participants. Figure 23 shows the Valsalva ratio of the VAD and manometer.

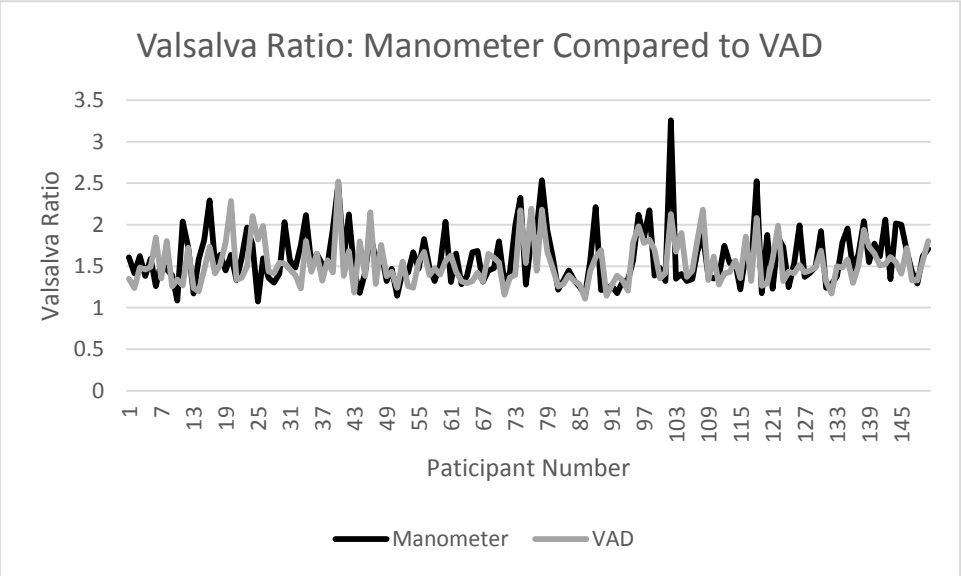

Figure 21 Valsalva Ratio Raw Data of the Manometer vs VAD

Figure 23 shows that the majority of the VAD and manometer Valsalva ratios are very similar. We assessed the mean of the Valsalva ratios to see if there was a true difference between the groups shown in figure 24.

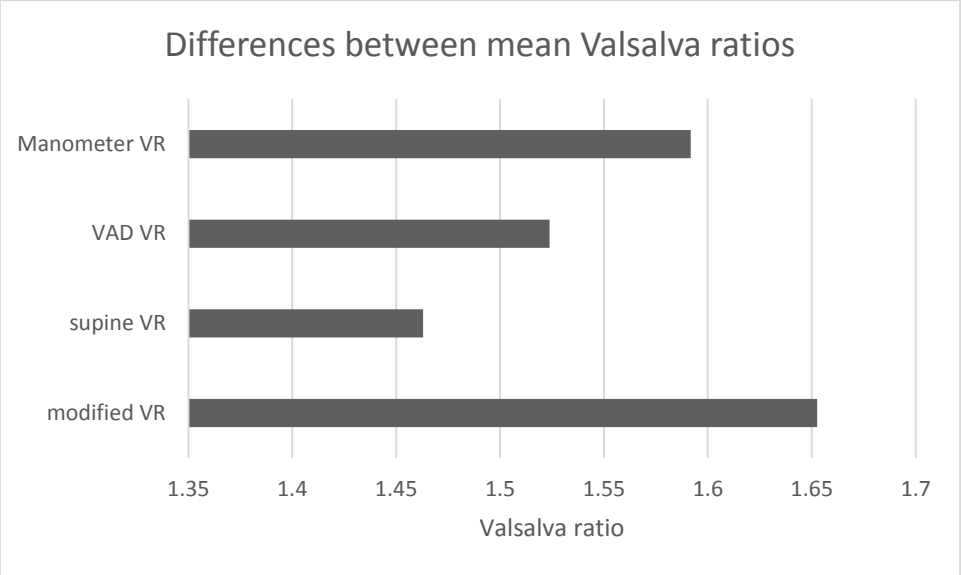

Figure 22 Valsalva Ratio

The modified VM has a much larger Valsalva ratio than any other group. Figure 24 shows that the manometer and the VAD had a difference in means of 0.07.

Statistical analysis

For the type of VM and the device analysis, we used a mixed linear regression. First we ran a model including an interaction term for type of device and manoeuvre to allow for the possibility that any difference between devices varied between manoeuvres (and vice versa). There was no evidence of such an interaction (p=0.70), hence we removed that term and included only main effects.

The next thing we examined was whether the order of VM had an effect when we inputted this data as a categorical variable and this was shown not to be significant (p=0.32). When inputted as a continuous variable (suggesting a linear change as we go from 1-4), it is just significant at p=0.049. However it makes very little difference to our estimates of the effect (or p values) of VM done and device used so we excluded this as a variable.

The independent variables included for the mixed linear regression were; type of device, type of VM and “person” as a random variable.

Supine VM was associated with a lower resting pre-VM heart rate, probably representing a higher degree of initial vagal tone in this starting position compared to the semi-recumbent position in the modified VM. In that case, it may arguably be relevant to consider the absolute reduction in heart rate without adjusting for the baseline rate. Re-running the model without the baseline, the modified VM was seen to have produced a greater reduction in heart rate than the supine VM by 7.7 bpm (5.6 to 9.8; $p<0.001$), while the comparison between devices no longer reached the traditional level of significance: the manometer reduced heart rate by 2.0 bpm more than the VAD (-0.1 to 4.1; $p=0.06$).

Pressure and duration of VAD and manometer

Table 13 shows the mean and range of pressures the VM reached and duration it was held in relation to the VAD and the manometer. However, due to the skewed data shown in figure 25 and 26, the mean is not a good representation of the pressure or duration achieved.

	VAD	Manometer
Pressure mean (mmHg)	42.46	39.96
Pressure range	30-50	25-50
Duration (s)	13.70	14.91 (14.99 exclude outliner)
Duration range	5-15	4-15

Table 12 Averages of Duration and Pressure

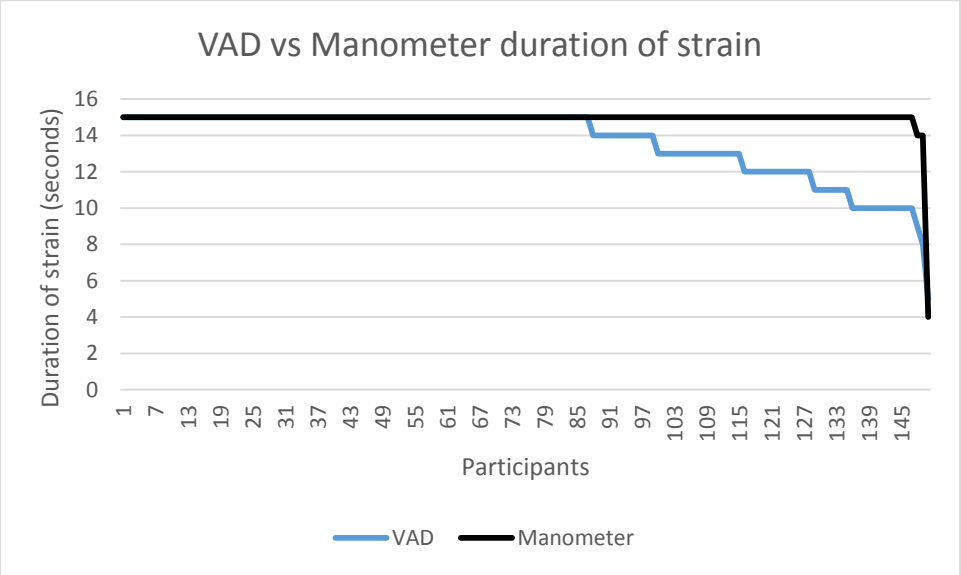

Figure 23 Raw Data of Pressure of Strain Duration

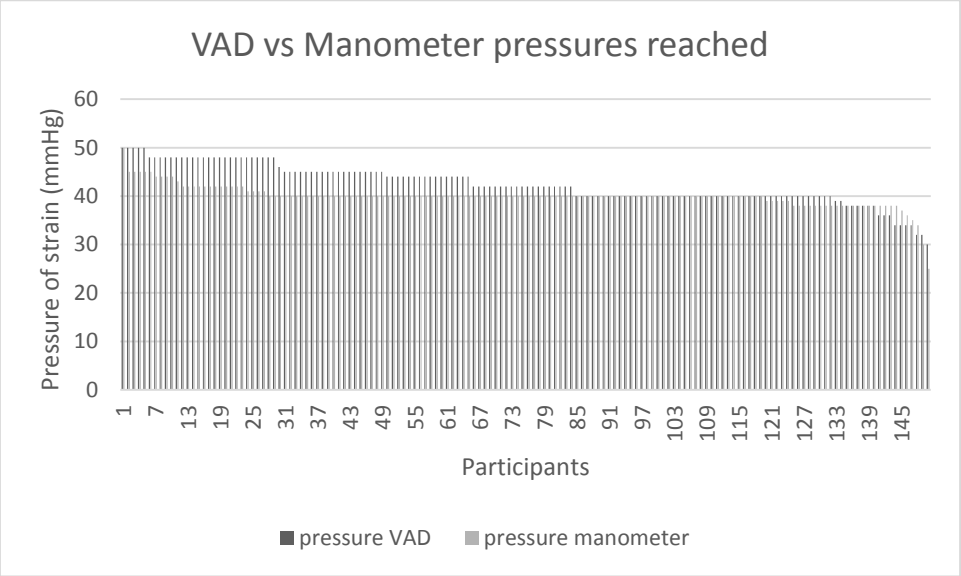

Figure 24 Raw Data of Pressures Achieved

Duration

We categorised the data according to duration, setting out whether 15 seconds was achieved or not. We examined whether the modified or supine positioning had any effect on duration, and it was shown to have no effect (data is shown in appendix E). Tables 14, 15 and 16 show the number of VMs that achieved a duration of 15 seconds = yes or <15 = no, with percentages shown below.

Supine VM:

Type_Device	RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Manometer	2	73	75
	2.67	97.33	100.00
VAD	29	46	75
	38.67	61.33	100.00
Total	31	119	150
	20.67	79.33	100.00

Table 13 Duration of Strain Achieved in the Supine Poistion

Modified VM:

Type_Device	RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Manometer	1	74	75
	1.33	98.67	100.00
VAD	34	41	75
	45.33	54.67	100.00
Total	35	115	150
	23.33	76.67	100.00

Table 14 Duration of Strain Achieved in the Modified Position

Overall:

Type_Device	RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Manometer	3	147	150
	2.00	98.00	100.00
VAD	63	87	150
	42.00	58.00	100.00
Total	66	234	300
	22.00	78.00	100.00

Table 15 Duration of Strain Achieved by the VAD and Manometer

People are less likely to achieve 15 seconds with the VAD than the manometer, independent of whether supine or modified VM. Overall the type of VM does not affect the ability to achieve 15 seconds, but the type of device does. Statistical analysis was undertaken using McNemar's test. The VAD was significantly less likely to produce a time of 15s compared to the manometer in the supine and the modified VM ($p<0.001$ and $p<0.001$). Examining the type of manoeuvre, the effect was not significant for either the supine VM or the modified VM ($p=0.15$, $p=0.13$).

Pressure

We analysed the pressures created, we grouped the data into two groups; achieving pressures of 35-45, or not achieving these pressures. We then compared the type of manoeuvre and the type of device used to see if either had an effect. We used a McNemar's test for assessing the statistical importance of the different pressures achieved. Table 17 and 18 show the number and percentage of VMs that are in the two groups.

VAD

Key
frequency *row percentage*

Type_VM	Pres 35-45 no	yes	Total
Supine	17 22.67	58 77.33	75 100.00
Modified	20 26.67	55 73.33	75 100.00
Total	37 24.67	113 75.33	150 100.00

Table 16 Pressures Achieved by the VAD

Manometer

Key
frequency *row percentage*

Type_VM	Pres 35-45 no	yes	Total
Supine	2 2.67	73 97.33	75 100.00
Modified	2 2.67	73 97.33	75 100.00
Total	4 2.67	146 97.33	150 100.00

Table 17 Pressures Achieved by the Manometer

The mean strain pressures delivered by manometer and VAD were similar (39.96 vs 42.46 mmHg). Regardless of the position of the VM (supine or modified), the manometer was more precise, with 97% of participants straining between 35-45mmHg compared to 75% when using the VAD.

On statistical analysis, it was shown that the type of manoeuvre did not affect the pressure (when using the manometer, $p=0.72$, when using device $p=1.0$). However, it was shown that the type of device did affect the pressure, with more people achieving the desired pressure with the manometer than the device ($p<0.001$ for both supine and modified VMs).

So, whether for supine or modified VM, people are more likely to produce >40mmHg with the VAD compared with the manometer. Examining the VAD in more detail, 30 people achieved 40mmHg when supine, compared to only 18 in the modified VM. With the modified VM there was an increased number of pressures over 45mmHg, as shown in table 19.

Peak Pressure (mmHg)	Type_VM		
	Supine	Modified	Total
30	1	0	1
32	2	0	2
34	3	1	4
36	2	1	3
38	6	0	6
39	1	1	2
40	30	18	48
42	5	14	19
44	8	8	16
45	6	13	19
46	1	0	1
48	8	16	24
50	2	3	5
Total	75	75	150

Table 18 Pressure Created by the VAD in Supine and Modifed Positions

Adverse events

22.7% of participants experienced adverse events, which was much higher than in previous studies. All of these adverse events were transient. No serious adverse events were exhibited. The number and type of adverse events are shown in table 20. The most common side effect was a headache and light-headedness. Some participants exhibited more than one side effect.

	The Modified VM		The Supine VM	
	VAD	Manometer	VAD	Manometer
Lightheaded	3	2	1	1
Tingling lips	1	0	0	1
Ectopic	1	0	0	0
Rib strain	1	0	0	0
Head rush	0	0	0	1
Unable to blow into tube	0	0	0	1
Headache	1	6	4	6
Vision changes	0	0	0	2
Chest discomfort	1	0	0	0
Device failure	0	0	1	0
Totals	8/75	8/75	6/75	12/75
Totals Modified and Supine	16/150		18/150	

Table 19 Side Effects of the Supine VM Compared to the Modified VM with Subgroups of VAD and Manometer.

The number of participants that exhibited adverse events is shown in table 21. Examining the raw data, it appears that the VAD exhibited less adverse events. We conducted a mixed-effects logistic regression with a binary outcome of “any side effect”. There was no statistical evidence determining whether the VM type or device type affected the risk of adverse events (p=0.80 type of VM, p=0.08 type of device).

Number of participants experiencing side effects		
Type of manoeuvre	Modified VM	Supine VM
VAD	8/75	6/75
Manometer	8/75	12/75

Table 20 No. of Participants Experiencing Side Effects

Chapter Six – Discussion and Conclusion

Discussion

Our results show that the modified VM is statistically superior to the supine VM at producing a reduction in heart rate, indicating the physiological advantage of the modifed VM. This was shown by the higher vagal response exhibited by the modified VM with a larger absolute and relative drop in heart rate compared to the supine VM. This is consistent with the increased effiicacy seen in previous clinical trials (2,55).

The modified VM is associated with a higher pre VM heart rate (probably due to an initial decrease in vagal tone in this position to maintain cerebral perfusion). The exaggerated changes to venous return resulting from the semi-recumbent position in the strain phase and leg elevation in the supine relaxation phase (Valsalva phase three) result in more intense vagal stimulation overall with the modified VM. This causes a greater drop in heart rate and a larger Valsalva ratio. Previous studies show that a larger Valsalva ratio correlates with a greater chance of SVT being terminated by the VM. (37)

This higher baseline heart rate in the modified VM significantly affects our statistical analysis, causing the initial adjusted mean drop in heart rate to be lower than expected. If we include this as a variable the coefficient is 3.7 bpm, however if we exclude it from the analysis the coefficient increases to 7.7 bpm ($p<0.001$). We believe 7.7 bpm is the true result as it shows the full drop in heart rate from the pre VM heart rate to post VM rate, showing the full level of vagal tone. In terminating SVT it is the vagal tone that terminates SVT not just the lowering of heart rate. This is part of the physiology behind the VM and is represented by a Valsalva ratio of 1.63. The Valsalva ratio has been shown to be a good predictor for the termination of SVT. The larger the vagal tone, the higher the chance of terminating SVT; therefore the pre VM heart rate should not be included as a variable. (37)

The Mehta study shows that a Valsalva ratio of >1.3 was very likely to terminate AVRT - 93% of participants terminated SVT on two out of three occasions, whereas with AVNRT this was shown to be less effective, only terminating 33%. (37) However this may be due to Mehta's method of creating the Valsalva ratio and not measuring phase two which is where the majority of retrograde terminations occur. (34) We included phase two within our measurement if any bradycardic response appeared there. The Mehta study had a higher termination rate than otherwise seen, though their Valsalva ratios peaked at 1.45 and both our ratios are much higher than this. This may indicate greater efficacy of our manoeuvres and the VAD.

The VAD did not perform quite as well as the manometer with the difference in drop of heart rate just reaching statistical significance. This coefficient (1.9 bpm including pre VM heart rate as a confounding factor) was less than our previously stated clinically meaningful difference of 4bpm (which was excluded from the 95% confidence interval). It is debateable whether this would affect cardioversion rates in practice. In our second analysis, which excluded the interaction of having a higher pre VM heart rate, the results changed very slightly creating a coefficient of 2.0, however the difference now becomes insignificant (p=0.06). This is important as there are modifications we can apply to the VAD to make it more efficient, which means it has the potential to be at least as efficacious as the manometer.

The Valsalva ratio of the VAD group is 1.52 compared to 1.59 of the manometer group, so, according to previous research the VAD should be effective in the termination of SVT. The benefit of having a small handheld device which is easy to use, by doctors, paramedics and patients, should give the VAD advantages over the manometer. The VAD should give a greater chance of termination from VM because the earlier a VM is carried out, the more effective it is. (6) An Australian paper showed that 92.8% of emergency doctors were unable to carry out a valid VM. (68) The VAD will also act as an aide-memoire for the modified VM and encourage its use in everyday practice.

The VAD was associated with significantly shorter strain duration than the manometer. Participants achieved an average strain duration of one second less with the VAD compared to the manometer. This is likely to be a result of the VAD's air leak causing participants to prematurely run out of breath. A small leak is thought important to ensure that the required intrathoracic pressure is used instead of oral pressure. (27). Anecdotally it was more noticeable in female participants who have a lower lung functional residual capacity ran out of breath faster, which supports the theory that this leak was the cause for the reduced strain duration observed. This degree of leak and shorter duration of VM strain might account for the device's marginally reduced effect on heart rate. This has been fed back to the manufacturer to consider refinements to the design.

This study's aim was to show a benefit of the VAD over the manometer, not a non-inferiority study. A non-inferiority study would show whether the manometer was the same as the VAD. A non-inferiority study requires many more people, but we believe it would show the VAD was not inferior to the manometer. This is because the results between the VAD and the manometer are very similar and with a small or no significance between them. We believe this difference will decrease in a non-inferiority study.

The aim of this study was to explore the potential benefit of the VAD over the manometer. It was not a non-inferiority study, as this this requires many more participants. We believe that, were this a non-inferiority study, the results would have indicated that the VAD is not inferior to the manometer, on the basis that the results were similar between the two methods. A formal study of this would be required to verify this belief.

The device produced a mean pressure of strain similar to the manometer. Although the variation of pressures was greater than with the manometer, this was within a clinically appropriate range and much better than that seen with use of a syringe. (5) Recording pressures was difficult due to the potential variability during the 15 seconds strain. The pressure recorded was the highest the participants were able to sustain for 5 seconds. The impact of measuring the

pressures achieved in this way could have introduced a bias into the study. It is not known how well this value correlates with the pressures achieved over the full 15 seconds, and serial or continuous measurements would have been able to improve the validity of the findings. While this was not feasible in this study, follow-up analyses could make use of this suggestion to further expand our knowledge of this topic.

Previously upright straining postures have been associated with a greater drop in blood pressure and therefore increased risk of syncope during straining; this complication was not seen in our study. This is consistent with previous trials assessing the modified VM. (2,55) Although there were no serious adverse events we had more non-serious adverse events than previously described. We believe this was because every participant was prompted after every strain for any possible side effect which may have increased participants' likelihood of commenting on their side effects and especially things they would not have otherwise mentioned. There were similar numbers of non-serious adverse events exhibited within each group, with no significant difference but a trend towards a lower number of adverse events in the VAD group.

The benefit of the VAD, with an aide memoire for the modified VM, is to hopefully see a reduction in the Emergency Department admissions of SVT as they will be cardioverted in the pre-hospital environment and left at home. We hope patients can have their own VADs to enable cardioversion at home.

We conducted our study on mainly young patients with a slight preponderance of females. This is the demographic of the population with SVT. There is a second peak of incidence in older age, often in patients with associated co-morbidities and so consideration should also be given to repeating this study and assessing device performance in the older population.

Limitations

This study has important limitations. We acknowledge that this study used healthy volunteers and not patients with SVT. The VAD needs to be tested on patients in SVT to prove its clinical effectiveness, at the moment we can only theorise the efficacy of the VAD. We also recognise that this is a single site study carried out in Exeter, with patients only from the surrounding area, so it is not fully representative of the country. A large proportion of our participants are university students so this may have an effect on our results as the VM is more effective in the younger population.

Our primary outcome of measuring RR intervals and pre VM baseline is inherently inaccurate. However, we blinded the investigator to minimise observer bias and reduced it further by repeating with a different blinded investigator who was not a part of the research team. (8)

Efforts were made to standardise the level of inspiratory effort preceding the expiratory strain made by subjects for all manoeuvres, however accurate control of this was not always possible. Hence, some error may have been introduced by this variable. (8)

Recording pressures was difficult due to the potential variability over 15 seconds, so we measured the peak pressure held for a few seconds and had one investigator to record results to improve standardisation. The VAD's pressures were observed to be highest at the beginning and dropped significantly at the end. This means the recorded pressures may be misleading of the pressure achieved for the full 15 seconds.

The results and alignment with previous studies suggest that our method is reliable. We examined similar studies previously reported, and our methodology is similar. We used advanced statistics to ensure the strength of our findings. Despite our limitations, we believe that our method and results are reliable.

Next stage

We are looking at other modifications to the VAD to try to improve its patient friendliness. We want to make some modifications to the window showing where to blow. We will create some mockups and use a focus group to decide which is best. Our options are to create a window, so the marker appears if you blow to the correct pressure, or to have a green section to blow the marker to. We will assess whether it will work for people that are sight impaired.

Planned future studies will assess the use of the VAD in clinical practice by ambulance services to see the effects of the VAD and the aide memoire (ClinicalTrials.gov registration no: NCT03514628). We created an aide memoir to demonstrate how to use the VAD for this study shown in figure 21.

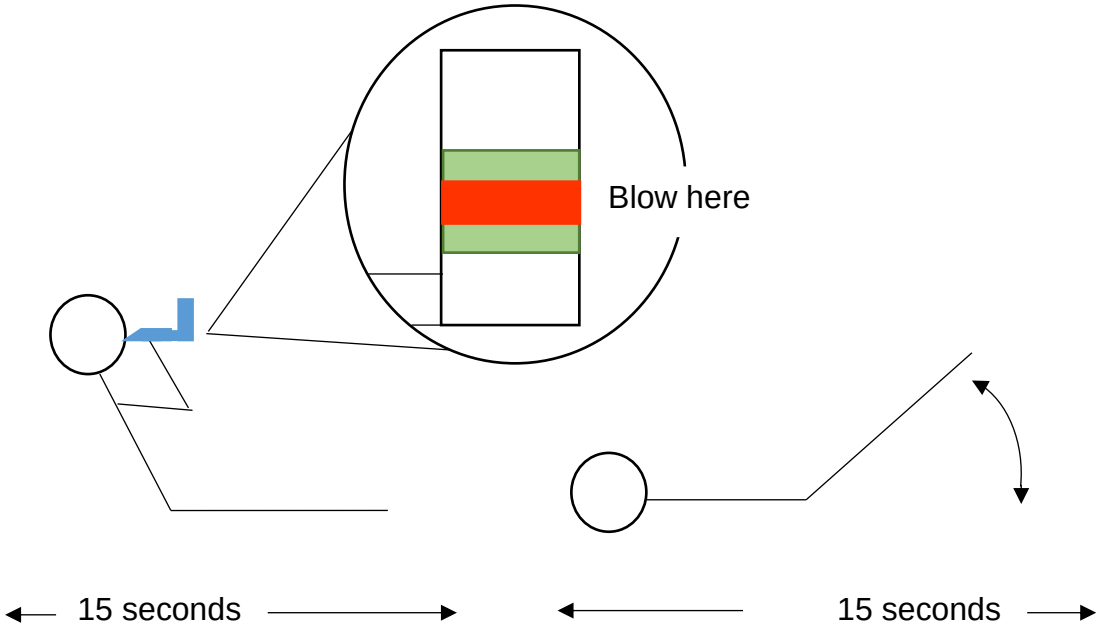

Figure 25 VAD aide memoire

I am also in the process of publishing the above results in the Emergency Medicine Journal (EMJ). This follows my first publication in the Emergency journal shown in Appendix H.

Conclusions

The findings in this study contribute to evidence supporting the efficacy of a modified VM producing a greater drop in heart rate than the supine VM. This confirms a physiological advantage (having a greater vagal response) with no increased risk of side effects and recommends the routine use of the modified VM.

The VAD was shown to safely generate the recommended VM strain with equivalent pressure to the manometer. Some simple modifications may enable the recommended duration of strain and the full effect to be achieved, as currently the manometer generates a slightly greater drop in heart rate than the VAD. However the VAD's benefits should outweigh this difference. The VAD's performance in patients with SVT remains to be tested.

Appendix A – Good Clinical Practice eLearning

NHS
National Institute for Health Research
Clinical Research Network

CERTIFICATE of ACHIEVEMENT

This is to certify that

Isabel FitzGerald

has completed the course

Introduction to Good Clinical Practice eLearning (Secondary Care)

July 26, 2017

Modules completed:

Introduction to Research in the NHS
Good Clinical Practice and Standards in Research
Study Set Up and Responsibilities
The Process of Informed Consent
Data Collection and Documentation
Safety Reporting

This course is worth 4 CPD credits

CPD

National Institute for Health Research
Clinical Research Network

Appendix B – Ethical Approval

UNIVERSITY OF EXETER | MEDICAL SCHOOL

University of Exeter Medical School
Research Ethics Committee

Certificate of Ethical Approval

Research Institute/Centre: Clinical Education

Title of Project: Testing of a Valsalva Assist Device (VAD) to assess effects on vagal tone and strain pressures achieved compared to a standard manometer in healthy volunteers performing standard and modified Valsalva manoeuvres

Name(s) of Project Research Team member(s): Andrew Appelboam and Izzy Fitzgerald

Project Contact Point: Andrew Appelboam

This project has been approved for the period

From: 15 August 2017

To: 31 July 2018

University of Exeter Medical School
Research Ethics Committee approval reference: Aug17/B/127

Signature: RGarside

Date: 15 August 2017

Name of Chair
Ruth Garside, PhD

Your attention is drawn of the attached paper "Guidance for Researchers when Ethics Committee approval is given", which reminds the researcher of information that needs to be observed when Ethics Committee approval is given.

Application Reference Number 17/06/127

UNIVERSITY OF EXETER | MEDICAL SCHOOL

University of Exeter Medical School
Research Ethics Committee

Certificate of Ethical Approval

Research Institute/Centre: Clinical Education

Title of Project: Testing of a Valsalva Assist Device (VAD) to assess effects on vagal tone and strain pressures achieved compared to a standard manometer in healthy volunteers performing standard and modified Valsalva manoeuvres
- ***Amendment to allow use of an alternative Valsalva device***

Name(s) of Project Research Team member(s): Andrew Appelboam and Izzy Fitzgerald

Project Contact Point: Andrew Appelboam

This project has been approved for the period

From: 30 October 2017

To: 31 July 2018

University of Exeter Medical School
Research Ethics Committee approval reference: Oct17/D/127Δ1

Signature: R Garside

Date: 30 October 2017

Name of Chair
Ruth Garside, PhD

Your attention is drawn of the attached paper "Guidance for Researchers when Ethics Committee approval is given", which reminds the researcher of information that needs to be observed when Ethics Committee approval is given.

Application Reference Number 17/06/127Δ1

Appendix C – Screening Protocol

Screening protocol

Date of screening ……

Participant screened:…… ……

Signature. …… Date ……

In the event of medical concerns on the day of screening which the research nurses deem require urgent attention: For advice please contact Dr Appelboam. In the event of a medical emergency redirect participants to the emergency department or call 999.

If participants have immediate concerns about their health and well-being they should contact health services as they normally would, through calling NHS 111 or attending the emergency department/calling 999 if it is a medical emergency.

- Please assure participants of the confidentiality of their answers, within the research study team.
- Please advise participants cannot participate if they have consumed alcohol or a stimulant drug within 24 hours or caffeinated drinks within 6 hours.
- **CONSENT SIGNED? Y/N**

• Date of Birth	
• Alcohol or stimulant drug in last 24 hours	
• Caffeinated drinks in last 6 hours	
• Gender	
• Smoker – if yes how many for how long	

- Ask participants to name any **medication** they are taking, dose and frequency. Please list here:

- **Ask participants if and of the following health conditions apply now or ever have in the past**

Could they be pregnant? (females)	Y / N	

Structural cardiac abnormalities	Y / N	
Any cardiac murmurs (Aortic stenosis)	Y / N	
Cardiac arrhythmias	Y / N	
Heart failure	Y / N	
Other heart problems	Y / N	
Respiratory disease (lung)	Y / N	
Hyperthyroidism	Y / N	
Vasculitis	Y / N	
Retinopathy	Y / N	
Glaucoma	Y / N	
Family history of sudden death	Y / N	
Unable to lie flat, or have legs raised greater than 45 degrees. E.g. prosethic hip	Y / N	

If the participant is unsure about whether any of the above apply please write notes in the right hand column

- Ask participants to name any **other past medical history.** Please list here:

- Vital signs (record these after the questionnaire has been completed):

Observations	**Values**	**Normal Ranges**

1. Heart Rate	Bpm	<100 Bpm
2. Respiratory Rate		11-20
3. Oxygen saturations	%	>96%
4. Blood Pressuren (systolic >100)		>100/60 systolic
5. Respiratory Exam		breath sounds normal/expansion
6. Cardiac Exam		heart sounds and rhythm
7. ECG		Regular sinus rhythm, narrow QRS complexes, no signs of ventricular hypertrophy or ischaemia

- **Anything observed** (irregular heartbeat, looks in anyway unwell)? Other comments

Appendix D – Standardised Instructions

Standardised instructions for doing procedure

There will be a total of 4 manoeuvres and your first one is –

In between each manoeuvre you will have two minutes after each repositioning to rest and allow your heart rate to return to normal and at least 3 minutes between each manoeuvre.

For the first 15 seconds, just sit and relax and I will count down to your first blow. Note if you run out of breath do not repeat the strain we will continue to the next part. We ask you to take a breath before each manoeuvre to ensure you have enough breath to complete it.

Manoeuvre 1 - *Supine VM using manometer*

You will be laid flat and asked to blow into the manometer at a pressure of 40mmHg (marked on machine) for 15 seconds, then continue to lie still for the next 15 seconds

Manoeuvre 2 - *Supine VM using* ***device***

You will be laid flat and asked to blow into the device aiming for a pressure of 55 (green zone) in one breath for 15 seconds, then continue to lie still for the next 15 seconds

Manoeuvre 3 - ***Modified*** *VM using manometer*

You will be laid at 45 degree angle and asked to blow into the manometer at a pressure of 40mmHg (marked on machine) for 15 seconds. As soon as the 15s are over you need to completely relax and allow yourself to be laid flat and have your legs raised to a 45 degree angle, then continue to lie still for the next 15 seconds

Manoeuvre 4 - ***Modified*** *VM using* ***device***

You will be sat at a 45-degree angle and asked to blow into the device aiming for a pressure of 55 (green zone) in one breath for 15 seconds. As soon as the 15s are over you need to completely relax and allow yourself to be laid flat and have your legs raised to a 45 degree angle, then continue to lie still for the next 15 seconds

It is important for all the manoeuvres that you get to appropriate pressure as soon as possible and try to hold it for the full 15 seconds. Note if you run out of breath do not take another breath but relax and lie still.

Device – the device will sometimes stop making a noise or the red line stop moving but do not worry and continue with the strain. The device has four holes in the top so is often harder to create the pressure, for the full 15 seconds so try and take enough breath to complete the strain.

Appendix E – Duration of Strain

Time grouped into <15 and 15. No-one went over 15, so this is essentially "did they achieve 15 seconds, yes or no".

With manometer:

Type_VM		RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Supine	No of Participants	2	73	75
	%	2.67	97.33	100.00
Modified	No of Participants	1	74	75
	%	1.33	98.67	100.00
Total	No of Participants	3	147	150
	%	2.00	98.00	100.00

With new device:

Type_VM		RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Supine	No of Participants	29	46	75
	%	38.67	61.33	100.00
Modified	No of Participants	34	41	75
	%	45.33	54.67	100.00
Total	No of Participants	63	87	150
	%	42.00	58.00	100.00

Overall:

Type_VM		RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Supine	No of Participants	31	119	150
	%	20.67	79.33	100.00
Modified	No of Participants	35	115	150
	%	23.33	76.67	100.00
Total	No of Participants	66	234	300
	%	22.00	78.00	100.00

So ability to achieve 15 seconds is not affected by type of VM, not for manometer nor for new device.

Appendix F – Duration of strain in VAD and Manometer

With manometer:

Type_VM		RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Supine	No of Participants	2	73	75
	%	2.67	97.33	100.00
Modified	No of Participants	1	74	75
	%	1.33	98.67	100.00
Total	No of Participants	3	147	150
	%	2.00	98.00	100.00

With new device:

Type_VM		RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Supine	No of Participants	29	46	75
	%	38.67	61.33	100.00
Modified	No of Participants	34	41	75
	%	45.33	54.67	100.00
Total	No of Participants	63	87	150
	%	42.00	58.00	100.00

Overall:

Type_VM		RECODE of Totaltimeofbreaths (Total time of breath (s)) No	Yes	Total
Supine	No of Participants	31	119	150
	%	20.67	79.33	100.00
Modified	No of Participants	35	115	150
	%	23.33	76.67	100.00
Total	No of Participants	66	234	300
	%	22.00	78.00	100.00

So ability to achieve 15 seconds is not affected by type of VM, not for manometer nor for new device.

Appendix G – Raw Data

Baselinemm	PostVMmm	Pre_Hrate	Post_Hrate	Diff_Hrate	Ratio_Hrate	Type_VM	Type_Device
163.5	20.5	76.72634	71.42857	5.297768	1.074169	Supine	Manometer
180	24	83.10249	75	8.102493	1.108033	Modified	New Device
156	25	60.12024	53.57143	6.548809	1.122244	Modified	New Device
159	22.5	81.52174	71.42857	10.09316	1.141304	Modified	New Device
177	24.5	96.15385	83.33334	12.82051	1.153846	Supine	New Device
200.5	32.5	77.12082	66.66666	10.45415	1.156812	Supine	Manometer
185	27	83.33334	71.42857	11.90476	1.166667	Modified	Manometer
199	29.5	89.82036	76.92308	12.89728	1.167665	Modified	Manometer
194.5	29	79.78723	68.18182	11.60542	1.170213	Modified	New Device
213.5	34	70.25761	60	10.25761	1.17096	Supine	New Device
206.5	26	60.60606	51.72414	8.881924	1.171717	Supine	Manometer
211.5	39	84.26966	71.42857	12.84109	1.179775	Modified	Manometer
161	23.5	80.64516	68.18182	12.46335	1.182796	Supine	New Device
155.5	21	75.37688	62.5	12.87688	1.20603	Modified	New Device
155	24	85.22727	69.76744	15.45983	1.221591	Modified	Manometer
156.5	28	70.92199	57.69231	13.22968	1.229315	Supine	Manometer
193	21	73.89162	60	13.89162	1.231527	Supine	New Device
185	24.5	81.08108	61.22449	19.85659	1.324324	Modified	New Device
194	27	62.63048	50.84746	11.78302	1.231733	Supine	Manometer
203	25	108.6957	88.23529	20.46037	1.231884	Supine	New Device
122	21	84.26966	68.18182	16.08784	1.235955	Modified	Manometer
146	25.5	80.64516	65.21739	15.42777	1.236559	Supine	Manometer
125	25.5	59.88024	48.3871	11.49314	1.237525	Supine	New Device
170	21.5	74.44169	60	14.44169	1.240695	Supine	New Device
247.5	29	88.75739	71.42857	17.32882	1.242603	Modified	Manometer
234	28	64.10256	53.57143	10.53113	1.196581	Modified	New Device
214.5	34	69.93007	44.11765	25.81242	1.585082	Modified	Manometer
250.5	31	79.5756	63.82979	15.74581	1.246684	Supine	Manometer
129.5	23	76.72634	61.22449	15.50185	1.253197	Supine	Manometer
144	21	91.74312	73.17073	18.57239	1.253823	Modified	New Device
130.5	30	52.35602	41.66667	10.68935	1.256544	Supine	New Device
127	22	66.22517	52.63158	13.59359	1.258278	Supine	New Device
193	27	72.63923	57.69231	14.94692	1.25908	Modified	Manometer
187.5	28.5	60.97561	48.3871	12.58851	1.260163	Supine	New Device
214	35	88.23529	69.76744	18.46785	1.264706	Supine	New Device
215	33	79.15567	62.5	16.65567	1.266491	Supine	New Device
140	25	85.22727	66.66666	18.56061	1.278409	Supine	New Device
139	22.5	80	62.5	17.5	1.28	Supine	Manometer
173	25.5	80	62.5	17.5	1.28	Supine	New Device
142.5	32.5	105.2632	46.15385	59.10931	2.280702	Modified	New Device
158	21.5	94.93671	69.76744	25.16927	1.360759	Modified	New Device
183.5	24.5	80	62.5	17.5	1.28	Supine	Manometer
163	26	76.92308	60	16.92308	1.282051	Supine	Manometer
179	24	62.1118	48.3871	13.7247	1.283644	Modified	New Device
133	28	81.96722	63.82979	18.13743	1.284153	Supine	New Device
142.5	28	81.96722	63.82979	18.13743	1.284153	Modified	Manometer
148	22	70.25761	54.54546	15.71216	1.288056	Supine	Manometer
139.5	24.5	63.42495	49.18033	14.24462	1.289641	Supine	New Device
141	22.5	69.12442	53.57143	15.55299	1.290322	Modified	Manometer

146	29	80.86253	62.5	18.36253	1.293801	Modified	New Device
151	27.5	59.76096	46.15385	13.60711	1.294821	Modified	New Device
195.5	21	82.87292	63.82979	19.04314	1.298342	Modified	New Device
153	22	88.75739	68.18182	20.57558	1.301775	Modified	Manometer
169	22	78.53403	60	18.53403	1.308901	Supine	Manometer
157.5	22.5	78.94736	60	18.94736	1.315789	Supine	New Device
176.5	24	82.41758	62.5	19.91758	1.318681	Supine	New Device
237.5	33.5	79.15567	60	19.15567	1.319261	Supine	New Device
215	33	76.14214	57.69231	18.44983	1.319797	Modified	New Device
233.5	36	76.14214	57.69231	18.44983	1.319797	Supine	Manometer
187	38	82.64463	62.5	20.14463	1.322314	Supine	New Device
207	30.5	96.77419	73.17073	23.60346	1.322581	Supine	Manometer
202.5	32	74.07407	46.875	27.19907	1.580247	Supine	Manometer
205	28.5	92.30769	69.76744	22.54025	1.323077	Supine	Manometer
182	27	92.59259	69.76744	22.82515	1.32716	Supine	New Device
138	17	75.18797	56.60378	18.5842	1.328321	Supine	New Device
122	22	75.18797	56.60378	18.5842	1.328321	Modified	New Device
144	25	83.10249	62.5	20.60249	1.32964	Modified	Manometer
127.5	27	79.78723	60	19.78723	1.329787	Modified	Manometer
216	35.5	78.32898	58.82353	19.50545	1.331593	Supine	New Device
237	36	83.33334	62.5	20.83334	1.333333	Supine	New Device
237	34	83.79888	62.5	21.29888	1.340782	Supine	Manometer
218	36	103.4483	76.92308	26.52519	1.344828	Supine	Manometer
138.5	21	122.449	90.90909	31.53989	1.346939	Supine	Manometer
162	21.5	96.46302	71.42857	25.03445	1.350482	Supine	New Device
159	25	59.76096	44.11765	15.64331	1.354582	Supine	New Device
184	28	92.59259	68.18182	24.41077	1.358025	Modified	New Device
123	24	84.98583	62.5	22.48583	1.359773	Supine	Manometer
180.5	45	91.46342	66.66666	24.79675	1.371951	Supine	New Device
175.5	25	85.95988	62.5	23.45988	1.375358	Supine	Manometer
185	46.5	82.87292	60	22.87292	1.381215	Supine	New Device
233.5	37.5	79.78723	57.69231	22.09492	1.382979	Modified	Manometer
253	35	59.28854	42.85714	16.43139	1.383399	Supine	New Device
216	36	62.89308	45.45454	17.43854	1.383648	Supine	New Device
193.5	41	86.7052	62.5	24.2052	1.387283	Modified	New Device
158.5	28.5	73.17073	52.63158	20.53915	1.390244	Modified	New Device
180	21	77.31959	55.55556	21.76403	1.391752	Supine	Manometer
186	22	75.94936	54.54546	21.40391	1.392405	Supine	Manometer
181	26	68.49315	49.18033	19.31282	1.392694	Supine	New Device
224.5	32	69.76744	50	19.76744	1.395349	Supine	New Device
217	41	73.52941	52.63158	20.89783	1.397059	Supine	New Device
200	43	77.72021	55.55556	22.16465	1.398964	Supine	New Device
238.5	33	82.41758	58.82353	23.59405	1.401099	Modified	Manometer
148	26	76.53061	54.54546	21.98515	1.403061	Modified	New Device
161	25.5	95.84665	68.18182	27.66483	1.405751	Modified	Manometer
148.5	25	105.6338	75	30.6338	1.408451	Supine	New Device
183	23.5	63.15789	44.77612	18.38177	1.410526	Supine	Manometer
174	23	86.20689	65.21739	20.9895	1.321839	Supine	Manometer
181	25	94.33962	66.66666	27.67296	1.415094	Modified	Manometer
174	25.5	88.49557	62.5	25.99557	1.415929	Modified	New Device
167.5	24	81.74387	57.69231	24.05156	1.416894	Supine	New Device
194.5	22.5	101.3513	71.42857	29.92278	1.418919	Supine	New Device

190.5	27.5	88.75739	62.5	26.25739	1.420118	Modified	New Device
201.5	25	63.69427	44.77612	18.91815	1.422505	Supine	Manometer
177	27.5	97.08738	68.18182	28.90556	1.423948	Modified	Manometer
192	32	85.47009	60	25.47009	1.424501	Supine	New Device
235.5	33.5	66.81515	46.875	19.94015	1.42539	Supine	Manometer
246	31	76.53061	53.57143	22.95918	1.428571	Modified	New Device
249.5	31	97.4026	68.18182	29.22078	1.428571	Supine	New Device
194.5	35.5	95.2381	66.66666	28.57143	1.428572	Modified	New Device
213.5	33	85.95988	60	25.95988	1.432665	Modified	New Device
224	33	87.7193	61.22449	26.49481	1.432749	Modified	Manometer
186	31	89.55224	62.5	27.05224	1.432836	Modified	New Device
194	27	77.31959	55.55556	21.76403	1.391752	Supine	New Device
186.5	27.5	80.42896	54.54546	25.8835	1.474531	Modified	New Device
183.5	24.5	92.02454	61.22449	30.80005	1.503067	Modified	Manometer
196	29	76.53061	51.72414	24.80647	1.479592	Supine	Manometer
224	34	71.77033	50	21.77033	1.435407	Supine	Manometer
210	33	82.87292	57.69231	25.18062	1.436464	Supine	Manometer
182	37	98.03922	68.18182	29.8574	1.437909	Supine	New Device
204	28.5	86.45533	60	26.45533	1.440922	Supine	New Device
213.5	27.5	92.02454	63.82979	28.19475	1.441718	Supine	New Device
196	28	78.74016	54.54546	24.1947	1.44357	Modified	Manometer
221	36	65.78947	45.45454	20.33493	1.447369	Supine	Manometer
190.5	31.5	88.75739	61.22449	27.5329	1.449704	Modified	New Device
185.5	24	90.63444	62.5	28.13444	1.450151	Modified	New Device
195	25	63.29114	43.47826	19.81288	1.455696	Supine	Manometer
188	26	104.1667	71.42857	32.73809	1.458333	Supine	New Device
189.5	25	64.37769	44.11765	20.26004	1.459228	Supine	New Device
150	25	100	60	40	1.666667	Supine	Manometer
182	24	81.08108	55.55556	25.52552	1.459459	Modified	New Device
169	24	93.1677	63.82979	29.33791	1.459627	Modified	Manometer
159	27	94.33962	55.55556	38.78407	1.698113	Modified	Manometer
157.5	26	95.2381	65.21739	30.02071	1.460317	Supine	New Device
191.5	25.5	86.20689	58.82353	27.38337	1.465517	Modified	Manometer
171	24.5	66.96429	45.45454	21.50974	1.473214	Supine	Manometer
191	25	72.46377	49.18033	23.28344	1.47343	Supine	New Device
173	25.5	86.7052	58.82353	27.88167	1.473988	Supine	Manometer
127	23	86.7052	58.82353	27.88167	1.473988	Supine	Manometer
149	23	65.35947	44.11765	21.24183	1.481481	Modified	Manometer
174.5	28	75.37688	50.84746	24.52943	1.482412	Supine	New Device
156	18	80.86253	54.54546	26.31708	1.48248	Modified	Manometer
154.5	22	82.41758	55.55556	26.86202	1.483516	Supine	New Device
162	22	101.3513	68.18182	33.16953	1.486487	Supine	New Device
162.5	21.5	84.26966	56.60378	27.66589	1.488764	Modified	New Device
155	36	67.72009	45.45454	22.26555	1.489842	Supine	Manometer
163.5	32.5	77.12082	51.72414	25.39668	1.491003	Supine	New Device
138	30	64.93507	43.47826	21.45681	1.493507	Supine	New Device
215	30	72.28915	48.3871	23.90206	1.493976	Supine	New Device
155	34	96.77419	44.11765	52.65655	2.193548	Modified	New Device
167.5	30.5	88.23529	58.82353	29.41176	1.5	Modified	New Device
187.5	24	94.63722	62.5	32.13722	1.514196	Modified	New Device
162.5	25	108.3032	71.42857	36.87467	1.516245	Modified	Manometer
128.5	28	66.96429	44.11765	22.84664	1.517857	Supine	Manometer

157.5	23	70.09346	46.15385	23.93961	1.518692	Supine	Manometer
148	29	80	52.63158	27.36842	1.52	Modified	New Device
142	36	81.52174	53.57143	27.95031	1.521739	Supine	Manometer
180	29	83.33334	54.54546	28.78788	1.527778	Modified	New Device
169	28.5	88.23529	57.69231	30.54298	1.529412	Supine	Manometer
178	26.5	69.76744	45.45454	24.3129	1.534884	Supine	Manometer
165.5	32	69.76744	45.45454	24.3129	1.534884	Modified	New Device
226.5	28.5	92.30769	60	32.30769	1.538462	Supine	New Device
241.5	31	88.75739	57.69231	31.06509	1.538462	Supine	Manometer
240	29	62.5	51.72414	10.77586	1.208333	Supine	Manometer
249	33	60.24096	45.45454	14.78642	1.325301	Modified	Manometer
188	25	64.23983	41.66667	22.57316	1.541756	Supine	New Device
197	26	100.6711	65.21739	35.45375	1.543624	Modified	New Device
219	30.5	96.77419	62.5	34.27419	1.548387	Supine	Manometer
228	33	105.6338	68.18182	37.45199	1.549296	Supine	Manometer
167	19.5	94.93671	61.22449	33.71222	1.550633	Modified	Manometer
180.5	20	68.49315	44.11765	24.3755	1.552511	Supine	Manometer
195.5	24.5	84.74577	54.54546	30.20031	1.553672	Modified	New Device
187.5	24	99.66777	63.82979	35.83798	1.561462	Modified	Manometer
163	23.5	95.84665	61.22449	34.62216	1.565495	Modified	New Device
169.5	37.5	82.41758	52.63158	29.786	1.565934	Supine	New Device
161.5	25.5	100	63.82979	36.17021	1.566667	Modified	New Device
165	26.5	85.47009	54.54546	30.92463	1.566952	Supine	New Device
180.5	30.5	81.08108	51.72414	29.35694	1.567568	Supine	Manometer
181.5	22	82.64463	68.18182	14.46281	1.212121	Supine	Manometer
176	21.5	71.42857	45.45454	25.97403	1.571429	Modified	New Device
184	21	94.33962	60	34.33962	1.572327	Modified	New Device
173	24	92.87926	58.82353	34.05573	1.578947	Supine	Manometer
187.5	24	107.9137	68.18182	39.73185	1.582734	Supine	New Device
189.5	24	93.1677	58.82353	34.34417	1.583851	Supine	Manometer
178	21	95.5414	60	35.5414	1.592357	Supine	New Device
173	23	86.7052	65.21739	21.48781	1.32948	Supine	New Device
192	25.5	78.125	58.82353	19.30147	1.328125	Supine	Manometer
199	24	92.02454	57.69231	34.33223	1.595092	Modified	Manometer
199	26.5	75.37688	56.60378	18.77311	1.331658	Modified	Manometer
144	28.5	106.383	66.66666	39.71632	1.595745	Modified	Manometer
132	28	96.15385	60	36.15385	1.602564	Supine	Manometer
151	27	85.95988	53.57143	32.38845	1.604584	Supine	New Device
185	29	64.23983	40	24.23983	1.605996	Supine	Manometer
188.5	41	90.90909	56.60378	34.30531	1.606061	Modified	New Device
165	30	83.33334	51.72414	31.6092	1.611111	Modified	Manometer
174	31	98.68421	61.22449	37.45972	1.611842	Supine	New Device
187	34.5	107.9137	66.66666	41.247	1.618705	Modified	Manometer
229.5	34	83.79888	51.72414	32.07475	1.620112	Supine	Manometer
225.5	30.5	66.51884	49.18033	17.33852	1.35255	Modified	New Device
242	33.5	61.98347	44.91018	17.07329	1.380165	Supine	Manometer
196	33	74.44169	45.45454	28.98714	1.637717	Supine	New Device
155	20.5	74.81297	46.15385	28.65912	1.620948	Supine	Manometer
110.5	36	97.4026	60	37.4026	1.623377	Supine	Manometer
148	21	67.87331	41.66667	26.20664	1.628959	Supine	New Device
131.5	28	70.09346	42.85714	27.23632	1.635514	Modified	Manometer
122.5	16.5	72.46377	44.11765	28.34612	1.642512	Modified	Manometer

152	25.5	69.44444	42.25352	27.19092	1.643518	Modified	Manometer
147.5	28	95.2381	57.69231	37.54579	1.650794	Modified	New Device
156.5	22	68.80734	41.66667	27.14067	1.651376	Modified	New Device
164	22.5	78.74016	47.61905	31.12111	1.653543	Modified	Manometer
180.5	24	112.782	68.18182	44.60014	1.654135	Modified	New Device
197	26	69.44444	41.66667	27.77777	1.666667	Modified	New Device
169	24.5	78.125	46.875	31.25	1.666667	Modified	Manometer
115.5	25.5	80.64516	48.3871	32.25807	1.666667	Modified	New Device
145.5	24.5	98.68421	58.82353	39.86068	1.677632	Supine	New Device
150	27.5	101.0101	60	41.0101	1.683502	Modified	Manometer
161.5	30.5	84.26966	50	34.26966	1.685393	Modified	Manometer
255	34	58.82353	44.11765	14.70588	1.333333	Supine	New Device
264.5	36.5	56.71077	41.09589	15.61488	1.379962	Supine	Manometer
244	33	61.47541	45.45454	16.02087	1.352459	Modified	Manometer
220	35.5	68.18182	42.25352	25.9283	1.613636	Modified	New Device
174.5	24	88.75739	52.63158	36.12581	1.68639	Supine	New Device
169.5	24	83.10249	49.18033	33.92216	1.689751	Supine	New Device
176	22.5	87.46355	51.72414	35.73942	1.690962	Modified	Manometer
186	32.5	101.6949	60	41.69492	1.694915	Modified	New Device
150.5	23.5	72.9927	42.85714	30.13556	1.703163	Modified	New Device
173.5	25	131.5789	76.92308	54.65587	1.710526	Supine	New Device
169	26	95.5414	55.55556	39.98585	1.719745	Modified	New Device
156.5	24.5	122.9508	71.42857	51.52225	1.721311	Modified	New Device
207	34	106.0071	61.22449	44.78257	1.731449	Supine	Manometer
239.5	29.5	118.1102	68.18182	49.92842	1.732283	Modified	New Device
199	37	104.1667	60	44.16666	1.736111	Supine	Manometer
251	34	102.7397	58.82353	43.91619	1.746575	Modified	Manometer
214	32.5	80.64516	46.15385	34.49132	1.747312	Modified	Manometer
162.5	41	107.5269	61.22449	46.30239	1.756272	Modified	Manometer
192.5	40	101.3513	57.69231	43.65904	1.756757	Modified	New Device
231	30.5	118.1102	66.66666	51.44357	1.771654	Modified	Manometer
251	32.5	88.75739	50	38.75739	1.775148	Modified	Manometer
184	34.5	115.8301	65.21739	50.61272	1.776062	Supine	Manometer
286.5	36	86.20689	48.3871	37.8198	1.781609	Supine	New Device
293	34.5	51.19454	43.47826	7.716278	1.177474	Supine	Manometer
157	25	107.1429	60	47.14286	1.785714	Supine	New Device
186	37	99.33775	55.55556	43.78219	1.788079	Supine	New Device
211.5	26	95.84665	53.57143	42.27522	1.789137	Modified	New Device
163	30	94.63722	52.63158	42.00564	1.798107	Modified	New Device
174.5	25	122.9508	68.18182	54.769	1.803279	Modified	New Device
181.5	24	118.1102	65.21739	52.89285	1.811024	Modified	Manometer
188	23.5	79.78723	63.82979	15.95744	1.25	Modified	Manometer
190.5	33	78.74016	45.45454	33.28561	1.732283	Supine	Manometer
154	22	108.6957	60	48.69566	1.811594	Modified	New Device
170	26	90.90909	50	40.90909	1.818182	Modified	New Device
158.5	24	89.55224	49.18033	40.37191	1.820896	Modified	Manometer
159.5	31.5	99.33775	54.54546	44.79229	1.821192	Supine	New Device
165.5	24	77.12082	42.25352	34.8673	1.825193	Modified	Manometer
167.5	24	89.55224	62.5	27.05224	1.432836	Modified	Manometer
187.5	25.5	80	58.82353	21.17647	1.36	Supine	Manometer
176	25	85.22727	60	25.22727	1.420455	Supine	New Device
207.5	35	100	54.54546	45.45454	1.833333	Supine	New Device

231	34.5	92.02454	50	42.02454	1.840491	Modified	Manometer
221.5	33	70.92199	38.46154	32.46045	1.843972	Modified	New Device
186	35.5	80.21391	43.47826	36.73565	1.84492	Supine	Manometer
188	22	75.37688	40.54054	34.83635	1.859297	Modified	New Device
186	23	81.52174	43.47826	38.04348	1.875	Modified	Manometer
183	23.5	92.87926	49.18033	43.69893	1.888545	Modified	Manometer
190	25	69.12442	36.58537	32.53905	1.889401	Modified	Manometer
169	30	90.63444	46.875	43.75944	1.933535	Supine	Manometer
197.5	27.5	121.9512	62.5	59.45122	1.951219	Supine	Manometer
182	27	101.3513	51.72414	49.62721	1.959459	Supine	Manometer
170	25.5	105.2632	53.57143	51.69173	1.964912	Supine	Manometer
139.5	27.5	107.5269	54.54546	52.98142	1.971326	Supine	Manometer
139	22	94.04388	47.61905	46.42484	1.974921	Modified	Manometer
185.5	27.5	104.1667	52.63158	51.53508	1.979167	Modified	New Device
181	23.5	102.7397	51.72414	51.01559	1.986301	Modified	New Device
175.5	26.5	91.74312	46.15385	45.58927	1.987768	Supine	Manometer
196	40	80.64516	40.54054	40.10463	1.989247	Modified	New Device
178	34.5	103.4483	51.72414	51.72414	2	Supine	Manometer
188.5	31	107.9137	53.57143	54.34224	2.014388	Modified	Manometer
114	19.5	80.21391	39.47368	40.74022	2.032086	Modified	Manometer
133	22	82.41758	40.54054	41.87704	2.032967	Modified	Manometer
127	22.5	120	58.82353	61.17647	2.04	Supine	Manometer
142	22	88.49557	42.85714	45.63843	2.064897	Modified	Manometer
179	29	77.92208	37.5	40.42208	2.077922	Modified	New Device
180	27.5	112.782	53.57143	59.21052	2.105263	Modified	New Device
169.5	35	117.6471	55.55556	62.0915	2.117647	Modified	Manometer
205	31	77.51938	36.58537	40.93401	2.118863	Modified	Manometer
139	28	113.6364	53.57143	60.06493	2.121212	Modified	Manometer
152	24.5	114.0684	53.57143	60.49701	2.129277	Modified	New Device
150	23.5	75	34.88372	40.11628	2.15	Modified	New Device
145	19.5	108.6957	50	58.69566	2.173913	Modified	New Device
142	20	79.5756	36.58537	42.99023	2.175066	Modified	Manometer
145	29	92.02454	42.25352	49.77102	2.177914	Modified	Manometer
178	30	116.7315	53.57143	63.16008	2.178988	Modified	New Device
157	27	129.8701	58.82353	71.0466	2.207792	Modified	New Device
199.5	26.5	88.49557	40	48.49557	2.212389	Modified	Manometer
217	28	114.9425	50	64.94253	2.298851	Modified	Manometer
209	30	100	41.66667	58.33333	2.4	Modified	Manometer
199.5	26.5	83.10249	33.33333	49.76916	2.493075	Modified	Manometer
154	25	81.08108	32.25806	48.82301	2.513513	Modified	New Device
138	25	92.30769	36.58537	55.72233	2.523077	Modified	Manometer
182	28.5	105.6338	41.66667	63.96714	2.535211	Modified	Manometer
171.5	29	135.7466	41.66667	94.07994	3.257919	Modified	Manometer

Appendix H – Letter to Editor – A Simple Device to Control Valsalva Manoeuvre Strain Pressure

Emergency. 2018; 6 (1): e22

OPEN ACCESS

LETTER TO EDITOR

A Simple Device to Control Valsalva Manoeuvre Strain Pressure; a Letter to Editor

Isabel FitzGerald[1], Andrew Appelboam[2]*

1. University of Exeter Medical School, St Lukes Campus, Heavitree Rd, Exeter, EX1 2LU, United Kingdom.
2. Emergency Department, Royal Devon and Exeter Hospital, Exeter, Devon, United Kingdom.

Received: February 2018; Accepted: April 2018; Published online: 10 April 2018

Cite this article as: A Simple Device to Control Valsalva Manoeuvre Strain Pressure; a Letter to Editor. Emergency. 2018; 6(1): e22.

Dear Editor:

We read with interest the article by Motamedi and colleagues about the use of a hand held manometer to measure strain pressure during Valsalva manoeuvre (VM) treatment of supraventricular tachycardia (SVT) (1). We also used a manometer in our study (REVERT) of a postural modification of the VM and are currently investigating the use of a simple, single patient use device to control VM strain pressure, NCT number:

NCT03298880 (2, 3). Such a device would be useful as blood pressure manometers are not always available and cannot be left with patients and other methods of generating the recommended strain such as syringes have been shown to be unreliable (4).

We note that Motamedi's study demonstrated a cardioversion rate of 14.8% in supine participants, which was similar to the rate achieved in the REVERT trial by control participants in the semi recumbent position (17%) (2).

In contrast, participants randomised to the modified VM in the REVERT trial, had a markedly improved cardioversion rate of 43% (2). This modification required participants to perform a 40 mmHg pressure strain for 15 seconds in a semi recumbent position but with supine repositioning and passive leg raise immediately after the Valsalva strain. To our knowledge this is the first trial to study this modification and was not described in the "new modified version" quoted and referenced in Motamedi's paper. To achieve the best cardioversion rates, we recommend use of a modified VM as described above with the strain controlled by a manometer where possible. A simple, single patient use device designed to deliver the recommended pressure may be helpful to facilitate this in practice and could be kept by patients for future use (3).

1. Appendix

1.1. Acknowledgements

Not Applicable.

1.2. Author's contribution

Isabel FitzGerald wrote and Andrew Appelboam edited the manuscript.

1.3. Conflict of interest

No Conflict of interests.

1.4. Funding and support

Not Applicable.

References

1. Motamedi M, Akbarzadeh MA, Safari S, Shahhoseini M. Valsalva maneuver using a Handmade Device in Supraventricular Tachycardia Reversion; a Quasi Experimental Study. Emergency. 2017;5(1):e81.
2. A Appelboam AR, C Mann, J Gagg, P Ewings, A Barton et al. Postural modification to the standard Valsalva manoeuvre for emergency treatment of supraventricular tachycardias (REVERT): a randomised controlled trial: The Lancet; 2015.
3. Testing of a Valsalva Assis Device (VAD) in Healthy Volunteers Performing a Valsalva Manoeuvre. ClinicalTrials-gov2018.
4. Thornton HS EM, Reynolds JA,Coats TJ. Valsalva using a syringe: pressure and variation. . 2016;33.

Glossary

Term	Definition
Cardioversion	Return of heart rhythm back to normal rhythm.
Carotid Sinus Massage	Gentle massage of the carotid artery on the side of your neck for 5 seconds (type of vagal manoeuvres).
Human Dive Reflex	A physiological reflex to immersion that causes physiological changes to conserve oxygen (type of vagal manoeuvre).
Manometer	Pressure gauge often used to measure blood pressure.
Modified VM	Participants performed the strain in the semi-recumbent position but immediately at the end of the strain, were laid flat and had their legs raised to 45° for 15 seconds. (2)
Observational Trial	A retrospective or prospective study which observes the natural course of events with or without a control group. (73)
Randomised Controlled Trial	Participants are randomly assigned to 2 (or more) groups, one group has a specific intervention with the other group having either a dummy intervention (placebo) or no intervention. Outcomes are accessed statistically. (73)
Repeated Measures Trial	Each participant is exposed to multiple conditions over time or under different conditions.
Retrospective Study	This study examines past exposure to a suspected risk factors for a disease or condition. (73)
Supine VM	Lying flat while completing a VM (for 15 seconds at pressure of 40mmHg).
Supraventricular Tachycardia	Abnormal rapid heart rate caused by electrical impulses originating above the heart's ventricles.
Systematic Review	A review summarises the evidence on a clearly formulated review question according to a predefined

	protocol, using systematic and explicit methods to identify, analyse and collate findings. (73)
Termination of SVT	SVT stops and the heart returns to normal rhythm.
Vagal Manoeuvres	A manoeuvre that stimulates the vagal nerve and causes a reflex bradycardia.
VAD	A purpose built device to create the correct pressure during a VM
Valsalva Manoeuvre	An exhalation against resistance, similar to blowing up a balloon.

Bibliography

1. **Resuscitation Council (UK)**. Peri-arrest arryhthmias. *Resuscitation Council (UK).* [Online] 2015. [Cited: 19 10 2017.] https://www.resus.org.uk/resuscitation-guidelines/peri-arrest-arrhythmias/.

2. **Appelboam A, Reuben A, Mann C, Gagg J, Ewings P, Barton A, et al.** *Postural modification to the standard valsalva manoeuvre for emergency treatment of SVT (REVERT): a randomised controlled trial.* Lancet. 2015;386(10005): 1747-53.

3. **Lim S, Anantharaman V, Teo W, Goh P, Tan A.** *Comparison of treatment of supraventricular tachycardia by valsalva maneuver and carotid sinus massage.* Ann Emerg Med. 1998;31(1): 30-5.

4. **Guy, Jeffrey.** *Pharmacology for the prehospital professional https://books.google.cl/books?id=knvfWlSFYPIC&pg=PA165&lpg=PA165&dq=adenosine+impending+doom&source=bl&ots=lKMqoVmmWe&sig=_E6BlsUOC739YjG_zzra5rey7Gg&hl=es&sa=X&ved=0ahUKEwjLkqut__baAhUGfpAKHaHHAlo4ChDoAQg5MAI.* 2010;165.

5. **Thornton H, Elwan M, Reynolds J, Coats T.** *Valsalva using a syringe: pressure and variation.* Emerg Med J. 2016;33(10): 748-9.

6. **Bronzetti G, Brighenti M, Mariucci E, Fabi M, Lanari M, Bonvicini M, et al.** *Upside-down position for the out of hospital managment of children with supraventricular tachycardia.* Int J Cardiol. 2018;252: 106-109.

7. **Whinnett Z, Sohaib S, Davies D.** *Diagnosis and management of supraventricular tachycardia.* BMJ. 2012;34(345): e7769.

8. **Wong LF, Taylor D, Bailey M.** *Vagal response varies with valsalva maneuver technique: A repeated-measures clinical trial in healthy subjects.* Ann Emerg Med. 2004;43(4): 477-482.

9. **Orejana L, Vidaillet H, DeStefano F, Nordstorm D, Vierkant R, Smith P, Hayes J.** *Paroxysmal supraventricular tachycardia in the general population. J Am Coll Cardiol.* 1998;31(1): 150-7.

10. **Bibas L, Levi M, Essebag V.** *Diagnosis and management of supraventricular tachycardias.* CMAJ. 2016;188(17-18):E466-E473.

11. **Appelboam A**. Emergency Medicine Consultant. Personal communication. 02 March 2017.

12. **Blomstrom-Lundqvist C, Scheinman M, Aliot E, Alpert J, Calkins H, Camm A, et al.** *ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias—executive summary. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology.* J Am Coll Cardiol, 2003;108(15): 11871-909.

13. **Porter M, Morton J, Denman R, Lin A, Tierney S, Santucci P et al.** *Influence of age and gender on the mechanism of supraventricular tachycardia.* Heart Rhythm, 2004;1(4): 393-6

14. **McGuire M, Bourke J, Robotin M, Johnson D, Meldrum-Hanna W, Nunn G, et al.** *High resolution mapping of Koch's triangle using sixty electrodes in humans with atrioventricular junctional (AV nodal) reentrant tachycardia.* Circulation, 1993;88(5): 2315-28.

15. **Issa Z, Miller J, Zipes D.** Atrioventricular Reentrant Tachycardia. *Clinical Arrhythmology and Electrophysiology.* Elsevier, 2009.

16. **Fish F, Kannankeril P, Johns J.** Disorders of Cardiac Rhythm. *Pediatric Critical Care.* Mosby, 2011.

17. **NHS, CKS -.** Scenario: Current palpitations . *NICE CKS.* [Online] 2015. [Cited: 2018 04 30.] https://cks.nice.org.uk/palpitations#!scenario.

18. **Smith G, Broek A, McD Taylor D, Morgans A, Cameron P.** *Identification of the optimum vagal manoeuvre technique for maximising vagal tone.* Emerg Med J. 2015;32(1):51-4

19. **The modified Valsalva maneuver - Video Review.** *Med Mastery.* [Online] Med review, 02 October 2015. [Cited: 19 03 2018]

https://www.medmastery.com/magazine/modified-valsalva-maneuver-video-review.

20. **Pstras L, Thomaseth K, Wanieswskl J, Balzani I, Bellavere F.***The Valsalva manoeuvre: physiology and clinical examples.* Acta Physiologica, 2016;217(2):103-19.

21. **Jellinek H.** *The Valsalva manoeuvre and Antionio Valsalva (1666-1723).* J R Soc Med. 2006;99(9): 448-451

22. **Smith G.** *Management of supraventricular tachycardia using the Valsalva manoeuvre: a historical review and summary of published evidence.* Eur J Emerg Med. 2012;19(6): 346-52

23. McGee S. Evidence based physical diagnosis. fourth edition. Philadelphia: Elsevier; 2017.

24. **Wang J, Wu C, Peng J, Patel N, Huang Y, Gao X et al.** *Early-Onset Convulsive Seizures Induced by Brain Hypoxia-Ischemia in Aging Mice: Effects of Anticonvulsive Treatments.* PLoS One, 2015;10(12): e0144113.

25. **Cohn A, Fraser F.** *Paroxysmal tachycardia and the effect of stimulation of the vagus nerves by pressure.* Heart. 1913;5: 93-105

26. **Nishimura R, Tajik A.***The Valsalva Maneuver - 3 Centuries Later..* Mayo Clin Proc. 2004;79(4): 577-8.

27. **Looga R.** *Reproducibility of the heart rate response to low-strain Valsalva manoeuvre in healthy subjects.* Respir Physiol Neurobiol. 2002;133(3): 251-8.

28. **Taylor D.***The Valsalva Manoeuvre a critical review.* SPUMS J. 1996;26(1).

29. **Roydhouse N.** *Letters to the Editor - The Valsalva Manoeuvre.* SPUMS J 1996;26(3).

30. **Looga R.** *The Valsalva manoeuvre - cardiovascular effects and performance technique: a critical review.* Respir Physiol Neurobiol. 2005;147(1): 39-49.

31. **Shindler D.** *Valsalva Maneuver and Echocardiography.* E-chocardiography Journal, 2002.

32. **Naoum C, Kritharides L, Gnanenthiran S, Martin D, Falk G, Yiannikas J.***Valsalva maneuver exacerbates left atrial compression in patients with large hiatal hernia.* Echocardiography. 2017;34(9): 1305-1314

33. **Tsai LM, Chen JH.** *Abnormal hemodynamic response to Valsalva maneuver in patients with atrial septal defect evaluated by Doppler echocardiography.* Chest. 1990;98(5): 1175-8 .

34. **Wen Z, Chen S, Tai C, Chiang C, Chiou C, Chang M.** *Electrophysiological Mechanism and determinants of Vagal Maneuvers for Termination of Paroxysmal Supraventricular Tachycardia.* Circulation. 1998;98: 2716-2723.

35. **Walker S, Cutting P.** *Impact of a modified valsalva manoeuvre in the termination fo paroxysmal supraventricular tachycardia.* Emerg Med J. 2009;27(4): 287-91

36. **Singer W, Opfer-gehrking T, Mcphee B, Hilz M, Low P.** *Influence of posture on the valsalva manoeuvre.* Clin Sci. 2001;100(4): 433-440

37. **Mehta D, Wafa S, Ward D, Camm A.** *Relative Efficacy of various physical manoeuvres in the termination of junctional tachycardia.* Lancet. 1988;331(8596): 1181-1185.

38. **Ekinci S, Akgul G, Ars E, Aydin A, Musalar E.** *Valsalva maneuvre techniques for supraventricular tachycardias: Which and how?* Hong Kong J Emerg Med. 2017;24(6): 298-302.

39. **Khurana R, Mittal D, Dubin N.** *Valsalva maneuver: shortest optimal expiratory strain duration.* J Community Hosp Intern Med Perspect, 2011;1(2).

40. **Majeed F, Yar T, Alsunni A, Alhawaj AF, ALRahim A, Alzaki M.** *Synergistic effect of energy drinks and overweight/obesity on cardiac autonomic testing using the Valsalva maneuver in university students.* Ann Saudi Med, 2017;37(3): 181-188.

41. **Gaspar J.***Comparing Valsalva manoeuvre with cartoid sinus massage in adults with supraventricular tachycardia. BestBETS Best Evidence Topics. 05 July* 2005. [Cited: 10 June 2018] https://bestbets.org/bets/bet.php?id=930

42. **Ballo P, Bernabo D, Faraguti S.** *Heart rate is a predictor of success in the treatment of adults with symptomatic paroxysmal supraventricular tachycardia.* Eur Heart J. 2004;25(15): 1310-7

43. **Collins N, Higgins G.** *Reconsidering the effectiveness and safety of carotid massage as a therapeutic intervention in patients with supraventricular tachycardia.* Am J Emerg Med. 2015;33(6): 807-9

44. Smith G, Morgans A, Boyle M. Use of the Valsalva manoeuvre in the prehospital setting: a review of the literature. Emerg Med J; 26(1).

45. **Waxman M, Wald R, Sharma A, Huerta F, Cameron D.** *Vagal techniques for termination of paroxysmal supraventricualr tachycardia.* Am J Cardiol. 1988;46(4): 655-664.

46. **Taylor D, Auble T, Yealy D.** *First-Line managemnet of paroxysmal supraventricular tachycardia.* Am J Emerg Med. 1999;17(2): 214-5.

47. **Sohinki D, Obel O.** *Current Trends in Supraventricular Tachycardia Management.* Ochsner J. 2014;14(4): 586-595.

48. **Camm J, Garratt C.** *Adenosine and Supraventricular tachycardia. N Engl J Med*. 1991;326:1221-1222.

49. **Rankin A, Brooks R, Ruskin J, McGovern B.** *Adenosine and the treatment of supraventricular tachycardia.* Am J Med. 1992;92(6): 655-664.

50. **Coli S1, Mantovani F, Ferro J, Gonzi G, Zardini M, Ardissino D.** *Adenosine-induced severe bronchospasm in a patient without pulmonary disease.* Am J Emerg Med, 2012;30(9): 2082.

51. (UK), Resuscitation Council. Adult Tachycardia (with pulse) algorithm. **Resuscitation Council (UK)**. [Online] october 2010. [Cited: 10 11 2017.] file:///C:/Users/if223/Downloads/G2010Poster_AdultTachycardia.pdf

52. BMJ Best Practice. BMJ Best Practice. [Online].; 2018 [cited 2018 08 26. Available from: https://bestpractice.bmj.com/topics/en-gb/537/treatment-algorithm.

53. NHS Choices. Supraventricualr tachycardia (SVT). **NHS choices**. [Online] NHS, 08 05 2015. [Cited: 10 11 2017.] https://www.nhs.uk/conditions/supraventricular-tachycardia-svt/treatment/.

54. J, Payne. Supraventricular Tachycardia in Adults. **Patient.** [Online] 01 12 2016. [Cited: 02 06 2018.] https://patient.info/doctor/supraventricular-tachycardia-in-adults#nav-6.

55. **Corbacioglu K, Akinci E, Cevik Y, Aytar H, Oncul M, Akkan S, et al.** *Comparing the success rates of standard and modified Valsalva maneuvers to terminate PSVT: A randomized controlled trial.* Am J Emerg Med. 2017;34(11): 1662-1665

56. **Motamedi M, Akbarzadeh M, Safari S, Shahhoseini M.** *Valsalva maneuver Using a Handmade Device in Supraventricular Tacycardua Reversion; a Quasi Experimental Study.* Emergency. 2017;5(1):e81

57. **Smith S, Taylor D, Morgans A, Cameron P** *Prehospital management of supraventricular tachycardia in Victoria, Australia: Epidemiology and effectiveness of therapies.* Emerg Med Australas. 2014;26(4): 350-5

58. **Chance JF, Warner JG, Elsawy T.** *Augmented Valsalva maneuver for supraventricular tachycardia in the young.* Ann intern Med. 1992;116(6): 523

59. Appelboam A, Gagg J, Reuben A. Modified Valsalva manoeuvre to treat recurrent supraventricular tachycardia: description of the technique and its successful use in a patient with a previous near fatal complication of DC cardioversion. BMJ Case Rep. 2014; bcr2013202699. Available from http://casereports.bmj.com/cgi/pmidlookup?view=long&pmid=25006052 [cited 18th February 2018].

60. **Taylor D, Wong L.** *Incorrect instruction in the use of the Valsalva manoeuvre for paroxysmal supra-ventricular tachycardia is common. Emerg Med Australas.* 2004;16(4): 284-87

61. **Smith G, Fry M, Taylor D, Morgans A, Cantwell K.** *Effectiveness of the valsalva manoeuvre for reversion of supraventricular tachycardia.* Cochrane Database Syst Rev. 2015;18(2):CD009502

62. **Wheeler J.** *Modified valsalva maneuver vs standard valsalva maneuver on emergency deparmtnet patient presentaing wiht SVT.* Shool of Physcian Assistant Studies, 2016:587

63. Philips E, Donofrio P. Autonomic Disorders, Encyclopedia of Neuroscience (autonomic disorders). Academic Press; 2009.

64. **Sharp, A.** *Clinical Guidline: Assessment and Management of Supraventricular Tachycardia.* South Western Ambulance Service (NHS Foundation Trust), 2018. CG21.

65. **Smith G, Boyle M.** *A cross-sectional study of victorian mobile intensive care ambulance paramedics knowledge of the valsalva manoeuvre.* BMC Emerg Med, 2009;14(9): 23

66. **Pstras L.** *Valsalva manoeuvre using a syringe: physics and implications.* Emerg Med. 2016;33(10): 831.

67. **Smith G, Boyle M.** *The 10ml syringe is useful in generating the recommended standard pressure of 40mmHg intrathoraccic pressure for the valsalva manoeuvre.* Emerg Med Australas. 2009;21(6):449-54.

68. **Honarbakhsh S, Baker V, Kirkby C, Robinson G, Antoniou S, Richmond L, et al.** *Safety and efficacy of paramedic treatment of regular supraventricular tachycardia: a randomised controlled trial.* Heart. 2017;103(18).

69. **Bhagat, K.** *Non-pharmacological termination of a supraventricular tachycardia.* Cent afr J Med. 1999;45(9): 246-7.

70. **Uber-Zak L, Venkatesh Y.** *Neurological complications of sit-ups associated with the valsalva maneuver: 2 case reports .* Phys Med Rehabil. 2002;83(2): 278 - 282.

71. Atef M. A rare complication of a therapeutic manoeuvre. BMJ case rep. 2009; bcr.06.2008.0027

72. **Stodtmeister R, Heyde M, Georgii S, Matthe E, Spoerl E.** *Retinal venous pressure is higher than the airway pressure and the intraocular pressure during the valsalva manoeuvre.* Acta Ophthalmologica. 2018;96(1): e68-e73

73. **NICE.** Glossary. *NICE.* [Online] [Cited: 14 June 2018.] https://www.nice.org.uk/glossary?letter=r.